W20: Ambulatory Urogynaecology

Workshop Chair: Linda Cardozo, United Kingdom

29 August 2018 08:35 - 11:35

Start	End	Topic	Speakers
08:35	08:40	Introduction	Linda Cardozo
08:40	08:55	Setting up an ambulatory service	Angie Rantell
08:55	09:10	Diagnostics in an ambulatory setting	Alex Digesu
09:10	09:25	Ambulatory management of OAB	Dudley Robinson
09:25	09:40	Ambulatory management of SUI	Roger Dmochowski
09:40	09:55	Ambulatory management of GSM	Stefano Salvatore
09:55	10:10	Ambulatory management of prolapse	Angie Rantell
10:10	10:25	Discussion	Linda Cardozo Angie Rantell Alex Digesu Dudley Robinson Roger Dmochowski Stefano Salvatore
10:25	10:35	Break	None
10:35	11:35	Hands-on session	Linda Cardozo Angie Rantell Alex Digesu Dudley Robinson Roger Dmochowski Stefano Salvatore

Aims of Workshop

To gain a theoretical and practical knowledge of all outpatient / office procedures available for women in the management of overactive bladder, stress incontinence, pelvic organ prolapse and urogenital atrophy.

Learning Objectives

- To understand the diverse applications of ambulatory procedures in urogynaecology.
- To understand the requirements in setting up an ambulatory service.
- To gain practical, hands-on experience in various ambulatory techniques.

Learning Outcomes

After the course, participants will appreciate the benefits of establishing an ambulatory urogynaecology service.

Target Audience

All health care professionals caring for women with lower urinary tract symptoms and pelvic floor dysfunction

Advanced/Basic

Basic

Conditions for Learning

Mixed lectures and hands-on opportunities with all the treatments discussed.

Suggested Learning before Workshop Attendance

Delegates should have an understanding of the current practices in their clinical setting and ideas of how they may like to enhance their current practice.

Suggested Reading

Incontinence 6th Edition Book.

Textbook of female urology and urogynaecology 4th edition Eds Cardozo & Staskin.

Introduction

Professor Linda Cardozo OBE, MD, FRCOG
King's College Hospital, London

The role of ambulatory care in the healthcare setting is increasing, not only due to the reduction in mortality and morbidity associated with procedures, but also the reduction in capital / staffing costs and increased tariffs associated with Ambulatory care making it a profitable service.

This workshop aims to discuss the role of Ambulatory care in a Urogynaecology setting. It will not only discuss how to set up services but will also provide theoretical and hands on demonstrations of all current diagnostics and treatments available to be performed for women with lower urinary tract symptoms, pelvic organ prolapse and genitourinary syndrome of the menopause. Each presenter has provided an abstract for their session and these are included below.

Setting Up an Ambulatory Service

Angie Rantell BSc (Hons), PGCert, NMP, RN
Lead Nurse, King's College Hospital

The success of any new service is dependent on the planning and support systems in place. In most cases these new services will require a change in staffing levels, equipment, consumables, funding, administration etc. This session will discuss the business planning that needs to be considered prior to setting up an ambulatory service including submitting business cases to apply for funding for new services, or how to encourage investment in equipemtn through appropriate coding and enhanced tariffs.. Different delivery models will be discussed including alternative staffing models etc. Governance and risk management for setting up new services will be addressed and along with a review of specific documentation that may need to be developed. Finally as with all new services, examples of audit and quality assessments will be suggested to review the new services in line with key targets / service drivers

Diagnostics in an ambulatory setting

Alex Digesu MD, PhD
Consultant in Obstetrics & Gynaecology Imperial College Healthcare NHS Trust

An ambulatory approach in urogynaecology offers advantages to both patients and providers, offering significant savings on service delivery.

A successful application of an ambulatory service depends on many factors such as patient selection, trained personnel, dedicated setting, specialized equipment. Ambulatory urogynaecological diagnostic procedures include: pad test, uroflowmetry, routine and ambulatory urodynamics, UPP, retrograde cystogram, imaging, cystoscopy.

Cystometry is the method by which the storage function of the lower urinary tract (LUT) is measured during the filling of the bladder. The aim of urodynamics is to find an objective, pathophysiological, explanation for the patient's LUT symptoms. Urodynamics is a replication of the LUT physiology in a laboratory situation and it is still considered the golden standard for LUT storage function assessment.

Pad testing is a non-invasive method of detecting and quantifying severity of urine leakage. The 4th International Consultation on Incontinence defined pad testing as ''an optional test for evaluation of urinary incontinence.'' Diverse testing durations have been reported in the literature and only for the 1-hr pad test a specific test protocol has been standardized. Although it is generally believed that longer tests are more reproducible, evidence on the accuracy of different methods of pad testing is inconsistent. A 24-hr test is more reproducible then a 1-hr test, but longer testing requires more preparation and a greater commitment on the part of the patient. A 24-hr testing is reported to be adequate in routine clinical settings while 48- to 72-hr testing is deemed necessary for clinical research. Performing this test in conjunction with a voiding diary, or simply recording fluid intake and frequency of incontinence episodes, will significantly increase its utility. A standard protocol for 24- to 72-hr pad testing does not exist at the present time. Despite the above limitations, the pad test provides objective assessment of involuntary urine loss.

Cystoscopes come in both flexible and rigid options. Rigid cystoscopes use the Hopkins rod-lens optical system which has the advantage of providing improved optical clarity when compared with the fiberoptic bundles used in flexible cystoscopes. However, this is becoming less noticeable with the adoption of flexible digital cystoscopes. Visualization is also enhanced in the rigid model due to greater irrigant flow rate. The advantage of the flexible scopes is that they are smaller in size and provide greater patient comfort, which is why they are used for routine flexible cystourethroscopy in the office setting. The flexible endoscope can also be passed easily with a patient in the supine position; whereas, in rigid cystoscopy, the patient must be in the frog-leg or lithotomy position. Another excellent advantage is the movement of the tip of the flexible cystoscope which allows for easier inspection of the bladder. With a rigid cystoscope, it is necessary to use multiple lenses with varying degrees of

angle to achieve proper inspection of the entire bladder. The AUA best practice policy statement on antimicrobial prophylaxis does not recommend antibiotic administration for routine diagnostic cystoscopy in the absence of patient-related risk factors.

Ambulatory Management of Overactive Bladder

Dudley Robinson MD FRCOG
Consultant Urogynaecologist, Kings College Hospital

Overactive Bladder (OAB) is the term used to describe the symptom complex of urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathology.

Whilst a conservative approach using life style modifications and drug therapy remains integral in the management of women with OAB many women will fail with initial management and require further investigation and treatment.
Recent advances in ambulatory care have revolutionised the care of patients with refractory OAB and the purpose of this lecture is to look appraise the evidence base for Botulinum Toxin and Percutaneous Tibial Nerve Stimulation (PTNS).

Botulinum toxin

Intravesical botulinum toxin, a neurotoxin derived from the anaerobic bacterium Clostridium Botulinum, may be an alternative for those women with intractable OAB. Botulinum toxin is postulated to work via several separate mechanisms but its exact action is not completely understood. It is thought to inhibit release of acetylcholine (ACh), Adenosine triphosphate (ATP) and substance P from the urothelium which have been implicated in mediating the intrinsic and spinal reflexes that lead to OAB. Botulinum toxin is also known to inhibit release of ACh from parasympathetic nerve endings, which leads to detrusor paralysis and consequently may reduce many of the symptoms of OAB. There is also an additional action on C-fibre afferents that is thought to be the mechanism behind the reduction in the sensation of urgency[i]. Botulinum toxin is injected into multiple sites in the detrusor muscle via cystoscopy (flexible or rigid) either under local or general anaesthesia.

Although botulinum toxin type A (BoNTA) is the most common subtype used, botulinum toxin type B is also effective in symptom reduction, but seems to be effective for a shorter period of time. A number of proprietary BoNTA preparations are commercially available. They are produced by very different isolation, extraction, purification, and formulation processes. Although all BoNTA products have the same serotype, their dose, efficacy, duration of effect and safety profile, are sufficiently different for them to be considered totally different compounds and not generically equivalent[ii]. Current evidence supports the short-term efficacy of 200 units of onabotulinumtoxin A in idiopathic detrusor overactivity (DO)[iii] and 300 units in neurogenic DO[iv]. However, there is a significant dose-related risk of voiding difficulties[v] , ranging between 8.9% (50 units) and 25.5% (300 units). A dose of 100 units may be the dose that appropriately balances symptom benefits with the post-void residual urine volume related safety profile for patients with idiopathic DO.

The effect of botulinum toxin may last for between three and 12 months, but robust evidence on long-term outcome is lacking[vi]. Whilst there are few studies regarding the efficacy and complications associated with repeat injections, the current data would suggest that repeat procedures are safe and remain effective[vii] .

Percutaneous Posterior Tibial Nerve Stimulation (PTNS)

Percutaneous Posterior Tibial Nerve Stimulation (PTNS) may be useful in those women with refractory OAB symptoms. The postulated mechanism of action for PTNS is through stimulation of the S3 sacral nerve plexus, using a retrograde pathway through direct stimulation of the posterior tibial nerve, accessed just above the ankle. PTNS involves insertion of a 34-gauge needle approximately 3-4 cm cephalad to the medial malleolus of the left or right ankle. A surface electrode is applied near the arch of the foot and the needle and electrode are connected to a low voltage electrical stimulator. The stimulation current is titrated to elicit curling of the big toe or fanning of all toes. It is usually offered as a course of 12 weekly, 30-min outpatient sessions. However, shorter courses with 12 stimulations performed at a rate of four per week have been reported in the literature[viii].

PTNS has been shown to be a safe and effective treatment option, with objective outcome comparable to that of pharmacotherapy[ix]. A recent systematic review and meta-analysis[x] reported a pooled subjective success rate of 61.4% (95% CI 57.5-71.8) and an objective success rate of 60.6% (95% CI 49.2-74.7). A significant drawback of PTNS in treating a chronic condition such as OAB is the need for repeated stimulations, as symptoms deteriorate by 6–12 weeks[xi]. There are limited long-term data in the literature with few studies looking at ongoing treatment over 12 months. A recent study has shown that with an average of 1.3 treatments per month, PTNS therapy is a safe, durable, and valuable long-term treatment option to sustain clinically significant OAB symptom control[xii].

Ambulatory Management of Stress Incontinence

Roger Dmochowski MD
Professor of Urology, Vanderbilt University

Urethral bulking therapy remains a reasonable, minimally interventive therapy for the treatment of stress or stress predominant mixed urinary incontinence in women. Given recent concerns related to more invasive procedures, urethral bulking therapy has experienced an increase in utilization for those women desirous of some intervention for their incontinence. A variety of agents exist and most developed countries will have access to at least two if not more types of agent. Currently biologic agents are no longer utilized. However this may change as recent autologous tissue bulking trials using stem cells are reported and are subjected to regulatory scrutiny. In the meantime, the choice of a variety of synthetic agents remains the backbone for this therapeutic modality. The convenience of an ambulatory procedure done under local anesthesia with relatively few adverse events (aside from transient retention and urinary tract infection) must be balanced against concerns related to therapeutic durability and need for repeat exposure for optimization of response. Additionally, it is critical to recognize that most of the recorded bulking trials are regulatory approval type trials with a rigorous standard of reporting to meet governmental requirements that often exceeds historical surgical reporting. A review of agents, potential unique complications, and realistic expectations as to durability and patient approbation will be summarized.

Ambulatory Management of GSM

Stefano Salvatore
Gynecology Department, San Raffaele Scientific Institute, Milan, Italy

The genitourinary Syndrome of Menopause (GSM) is a relatively new terminology, introduced in 2014, to describe tissue changes and symptoms related to the lower genital and urinary tract secondary to oestrogen deficiency. Both tracts, in fact, share a common embryologic origin and present oestrogen receptors. The symptoms secondary to GSM include vaginal dryness, itching, burning, dyspareunia, dysuria, urgency and urgency and stress urinary incontinence.

GSM can be treated by local oestrogens, SERMs like Ospemiphene, lubricants and moistoreizers. In the past few years many other approaches have been proposed, all based on regenerative medicine concepts and performed in an ambulatory setting.
Of these new treatments we can divide two groups: one using different forms of energy with the aim bio-activating tissue; and the other using components/elements stimulating tissue regeneration.

The former group includes laser technology, specifically erbium and CO2 lasers, radiofrquency (monopolar, bipolar and quadripolar). The latter group includes hyaluronic acid, platelet rich plasma (PRP) and stem cells.
All these possibilities are promising and widely used although, in many cases, a good evidence is still lacking. Moreover different treatments have been proposed for specific and/or all the symptoms of GSM.

In this workshop I will try to provide information about the rational often based on previous use in other fields of medicine. The postulated mechanism of action and the way it has been proved for each specific treatment will be reported together with evidence on histological changes in the treated tissues.

Data published in peer reviewed literature in treating vulvo-vaginal atrophy, sexual dysfunction and lower urinary tract symptoms related to GSM after menopause will be described. Contraindications, safety data and possible side effects/complications will be illustrated.

For some procedures a video, on how a specific procedure should be performed, will be shown. In all cases, however, a technical description will be provided including ho patients should be prepared before the procedure and which suggestions or prescriptions deliver to the patients.

Ambulatory Management of Pelvic Organ Prolapse

Angie Rantell BSc (Hons), PGCert, NMP, RN
Lead Nurse, King's College Hospital

Pelvic organ prolapse (POP) is a very common condition, particularly among older women. It is estimated that 50% of women who have children will experience some form of prolapse in later life, but because many women do not seek help the prevalence is unknownxiii. It is generally the symptoms associated with prolapse eg bladder, bowel and sexual dysfunction that motivate women to seek medical help. Prolapse accounts for 20% of women on the waiting list for gynaecological surgeryxiv.

POP is defined primarily as anatomical change, ie the downward displacement of a pelvic organ or the different vaginal compartments and their neighboring organs.xv. Symptoms include vaginal bulging, pelvic pressure and low backache. Women may also develop prolapse related lower urinary tract symptoms and prolapse related anorectal dysfunction symptoms. Pelvic Floor Muscle Training (PFMT) is often considered as the first line in management of urogenital prolapse. Individualised PFMT for women with prolapse is offered by specialist women's health physiotherapistsxvi and includes teaching pelvic floor exercises, vaginal examination and provision of advice regarding lifestyle changes. It may also include the use of biofeedback or neuromuscular electrical stimulation.

However, if this does not manage the symptoms of POP appropriately more invasive procedures are considered. At present there is a lot of controversy in the media surrounding the use of mesh in POP surgery as this is leading to many women wanting to avoid invasive surgery. For many of these women, following appropriate counselling regarding native tissue repairs they may go ahead with surgery but many wish to consider a less invasive management strategy. This may also be the only options for women who are unfit for surgery.

This presentation will discuss the conservative management of POP that can be performed in an ambulatory setting including the use of biofeedback and adjuvant devices. Intra-vaginal pessaries to support or occupy space in the vagina will be described as well as recommendations for which pessaries are suitable for each different type of POP. For those that are unable to retain a pessary, body worn devices will be considered. Finally, an overview of potential new therapies including the use of laser therapy to treat POP will be reviewed.

---

[i] Apostolidis A, Dasgupta P, Fowler C. Proposed mechanism for the efficacy of injected botulinum toxin in the treatment of human detrusor overactivity. Eur Urol 2006; 49: 644–50

[ii] Chapple C. Which Preparation of Botulinum Toxin A Should Be Used, Where Should It Be Injected, and How Should Its Efficacy Be Assessed? Eur Urol 2012; 61: 936-938

[iii] Tincello DG, Kenyon S, Abrams KR, Mayne C, Toozs-Hobson P, Taylor D et al. Botulinum Toxin A Versus Placebo for Refractory Detrusor Overactivity in Women: A Randomised Blinded Placebo-Controlled Trial of 240 Women (the RELAX Study). Eur Urol. 2012; 62: 507-514

[iv] Herschorn S, Gajewski J, Ethans K, Corcos J, Carlson K, Bailly G et al. Efficacy of botulinum toxin A injection for neurogenic detrusor overactivity and urinary incontinence: a randomized, double-blind trial. J Urol. 2011; 185: 2229-2235

[v] Dmochowski R, Chapple C, Nitti V, Chancellor M, Everaert K, Thompson C et al. Efficacy and safety of onabotulinum toxin A for idiopathic overactive bladder: a double-blind, placebo controlled randomised dose ranging trial. J Urol 2010; 184: 2416-2422.

[vi] Duthie JB, Vincent M, Herbison GP, Wilson DI, Wilson D. Botulinum toxin injections for adults with overactive bladder syndrome. Cochrane Database Syst Rev. 2011: CD005493

[vii] Dowson C, Watkins J, Khan MS, Dasgupta P, Sahai A. Repeated botulinum toxin type A injections for refractory overactive bladder: medium-term outcomes, safety profile, and discontinuation rates. Eur Urol 2012; 61: 834-839

[viii] Klingler HC, Pycha A, Schmidbauer J, Marberger M. Use of peripheral neuromodulation of the S3 region for treatment of detrusor overactivity: a urodynamic-based study. Urology 2000; 56: 766-771

[ix] Peters KM, Macdiarmid SA, Wooldridge LS, Leong FC, Shobeiri SA, Rovner ES et al. Randomised trial of percutaneous tibial nerve stimulation versus extended release tolterodine: results from the overactive bladder innovative therapy trial. J Urol 2009; 182: 1055-1061.

[x] Burton C, Sajja A, Latthe PM. Effectiveness of percutaneous posterior tibial nerve stimulation for overactive bladder: A systematic review and meta-analysis. Neurourol Urodyn 2012; 31: 1206-1216

[xi] van der Pal F, van Balken MR, Heesakkers JP, Debruyne FM, Bemelmans BL. Percutaneous tibial nerve stimulation in the treatment of refractory overactive bladder syndrome: is maintenance treatment necessary? BJU Int. 2006; 97: 547-50.

[xii] Peters KM, Carrico DJ, Macdiarmid SA, Wooldridge LS, Khan AU, McCoy CE et al. Sustained therapeutic effects of percutaneous tibial nerve stimulation: 24-month results of the STEP study. Neurourol Urodyn. 2012 Jun 5 [Epub ahead of print]

[xiii] Maher C, Baessler K, Barber M et al (2013) Surgical management of pelvic organ prolapse. In: Abrams C, Khoury W (eds) 5th International Consultation on Incontinence. Health Publication Ltd, Paris

[xiv] *Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence.* Obstet Gynecol 1997*;89:501–6.*

[xv] Haylen, B.T., Maher, C.F., Barber, M.D., Camargo, S., Dandolu, V., Digesu, A., Goldman, H.B., Huser, M., Milani, A.L., Moran, P.A. and Schaer, G.N., 2016. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic organ prolapse (POP). *Neurourology and Urodynamics*, *35*(2), pp.137-168.

[xvi] Hagen S, Stark D, Cattermole D (2004) A United Kingdom-wide survey of physiotherapy practice in the treatment of pelvic organ prolapse. Physiotherapy 90(1):19–26

Imperial College Healthcare NHS Trust

ICS 2018 PHILADELPHIA

Diagnostics in an ambulatory setting

ALEX DIGESU
Imperial College London - UK

Diagnostics in an ambulatory setting

ICS 2018 PHILADELPHIA

- ❑ Frequency Volume Chart, urinalysis and MSU
- ❑ Pad test
- ❑ Urodynamics
  - Simple: Uroflow, Post void residual
  - Basic: Filling cystometry, Voiding cystometry
  - Complex: Videourodynamics, Urethral pressure profilometry
  - Advanced: Ambulatory urodynamics
- ❑ Imaging
- ❑ Cystoscopy
- ❑ Neurophisiological testing

ICS 2018 PHILADELPHIA

Affiliations to disclose†:

ICS Board of Trustee
ICS Educational Committee
ICS Urodynamics Committee
ICS Institute Steering Committee
Associate Editor Neurourology and Urodynamics Journal
IUGA Academy Chair
Investigator for Bluewind Trial
Medtronic

† All financial ties (over the last year) that you may have with any business organisation with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

- ☐ Self-funded
- ☐ Institution (non-industry) funded
- [x] Sponsored by: International Continence Society

Frequency volume chart

ICS 2018 PHILADELPHIA

DATE/TIME	LIQUID INTAKE	VOLUME OF URINE	LEAKS	PAD
21.02.06			☆	
0215		150		
0715		250		
0800	Mug coffee 250ml			
0820		60	☆	P
0930	Cup Orange juice		☆	
1000		100		
1200	2 mugs coffee			
1400		300		
1430		20		
1530	Cup of Tea 200ml		☆	P
1600		100	☆	
1800	Cup of Tea 200ml			
1900		100		
2000	Glass Beer 200ml	20		
2030	Glass wine 50ml		☆	
2200				P
2300		150		

Record / Diary of:
Fluid intake
Voided volumes
No of voids
Incontinence/urgency
Pad

What is normal?

ICS 2018 PHILADELPHIA

- 151 asymptomatic women
- 19 -81 yrs
- 48 hour FVC

	Mean	Range
Frequency	**5.8**	**3 - 11**
Total voided vol (ml /24hrs)	**1430**	**600 -3100**
Mean void (ml)	**250**	**90 -610**
Largest void (ml)	**460**	**200 - 1250**

Larsson & Victor (1988)

Frequency / Volume Charts

ICS 2018 PHILADELPHIA

How long? 1,2,3,4,5,7,14 days

- Compare **1st week** results with subsequent week in **14 day** chart - good correlation
  Wyman et al 1988
- Compare **1st day** results with subsequent **5 days** - good correlation but total voided volume varied
  Barnick et al 1993
- Most units use 3 - 7 days
- Should represent home and work

Frequency / Volume Charts

ICS 2018 PHILADELPHIA

Patterns

- Normal volumes / normal frequency **Normal/USI**
- Normal volumes / increased frequency **Excess intake**
- Reduced volumes – fixed frequency **BPS**
  – variable frequency **DO**

Klevmark 1989

Frequency / Volume Charts

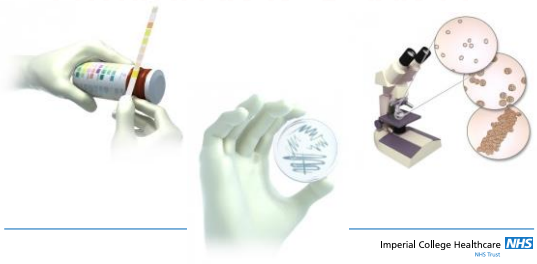
ICS 2018 PHILADELPHIA

So, are they useful?

- Fluid intake
- Symptom severity
- Bad voiding patterns
- Monitor effects of drug treatment
- Bladder retraining
- FVC has poor discriminatory value

ICS 2018 PHILADELPHIA

URINALYSIS & MSU



Imperial College Healthcare NHS

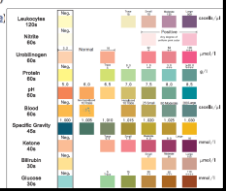
Urinalysis

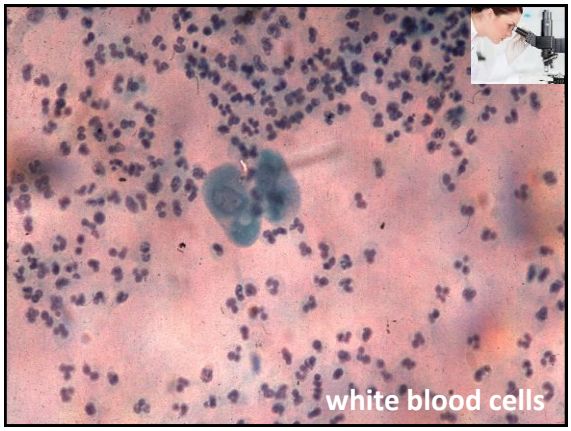
ICS 2018 PHILADELPHIA

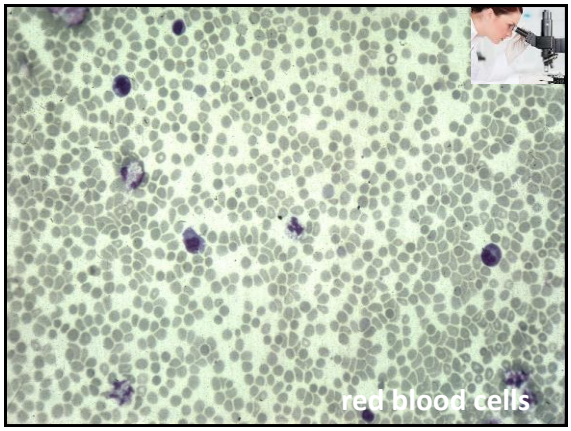
What substances can a rapid urine test detect?

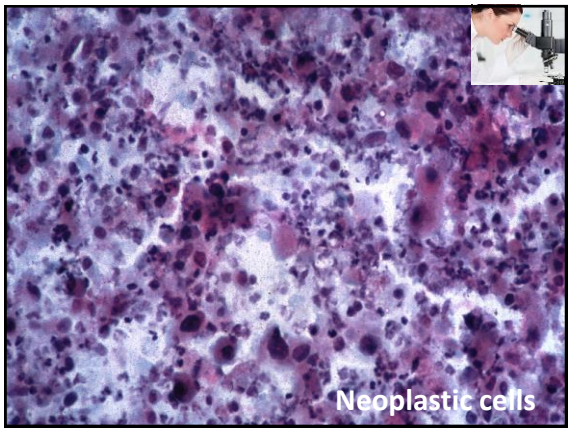
Many substances are usually found only in certain amounts in urine, so higher or lower levels indicate a deviation from the norm. The following substances can be checked using a rapid urine test:

- pH value (measure of the acidity of the urine. Normal values, depending on diet, range from about 5 to 7, where values under 5 are too acidic, and values over 7 are not acidic enough)
- Protein (not usually found in urine)
- Sugar (glucose, not usually found in urine)
- Nitrite (not usually found in urine)
- Ketone (a metabolic product, not usually found in urine)
- Bilirubin (breakdown product of hemoglobin, not usually found in urine)
- Urobilinogen (breakdown product of bilirubin, not usually found in urine)
- Red blood cells (erythrocytes, not usually found in urine)
- White blood cells (leukocytes, not usually found in urine)









Pad weight testing

ICS 2018 PHILADELPHIA

- Qualitative assessment (continent vs incontinent)
- Quantitative assessment (how much)

- Weight of the pads before and after test
- Weight gain in g = urine loss in mls

Short term tests	Long term tests
20 min – 2 hrs	12 hrs – 72 hrs
qualitative assessment	quantitative assessment

ICS pad weight test

ICS 2018 PHILADELPHIA

Only 1 hour pad weight test is standardized[1]

0 -15 min:	drinking of 500 ml sodium-free liquid, resting
15 - 45 min:	walking, including stars climbing to one flight up & down
45 - 60 min:	standing up from sitting (10 times) coughing vigorously (10 times) running on the spot (1 min) bending to pick up small object from the floor (5 times) washing hands in running water (1min)

[1]Seventh report on the standardisation of terminology of lower urinary tract function: lower urinary tract rehabilitation techniques. International Continence Society Committee on Standardisation of Terminology. Scand J Urol Nephrol, **26:** 99, 1992

Performing the pad weight test

ICS 2018 PHILADELPHIA

Short term tests	Long term tests
sensitivity: 34-83%	sensitivity: no sufficient data
specificity: 65-89%	specificity: no sufficient data

Cut-off values

Short term tests	Long term tests
weight gain > 1g[1]	weight gain > 4g/24hrs[1]

[1]Staskin D, Kelleher C, Bosch R, Coyne K, Cotteril N, Emmanuel A, Yoshida M, Kopp Z: Initial assessment of urinary and faecal incontinence in adult male and female patients. In: Incontinence. Ed.:Abrams P, Cardozo L, Khoury S, Wein A. 4th Ed. Health Publ.Ltd, Paris 2009, pp 333-412

Quantification of the incontinence severity using the pad weight test

ICS 2018 PHILADELPHIA

	1-hour test	*24-hour test*
Mild incontinence	< 10 mL	< 20 mL
Moderate incontinence	11-50 mL	21-74 mL
Severe incontinence	>50 mL	>75 mL

O´Sullivan R, Karantanis E, Stevermuer TL, et al.: Definition of mild, moderate and severe incontinence on the 24-hour pad test. BJOG 2004; 111: 859-862

Uroflometry

ICS 2018 PHILADELPHIA

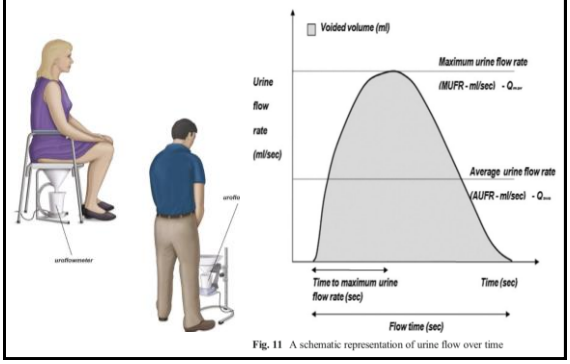


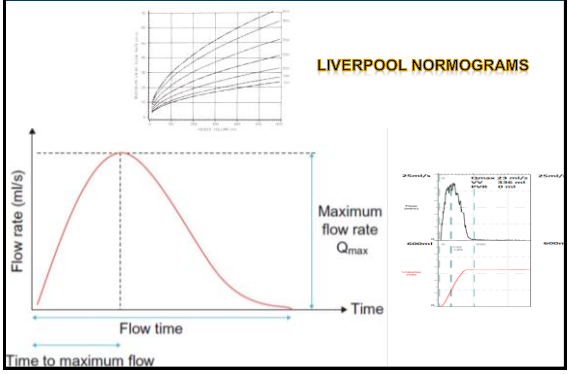
Fig. 11 A schematic representation of urine flow over time

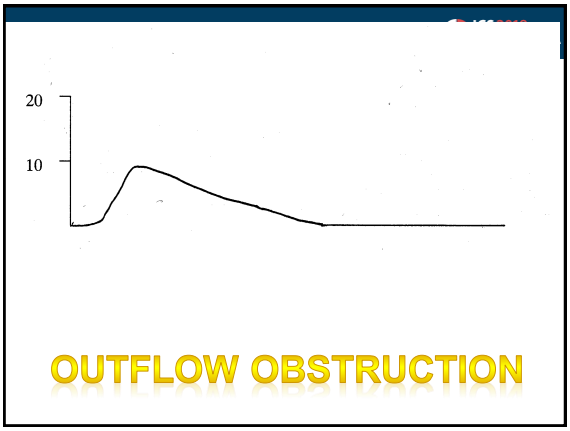
Normal flow rates (VV > 150ml)

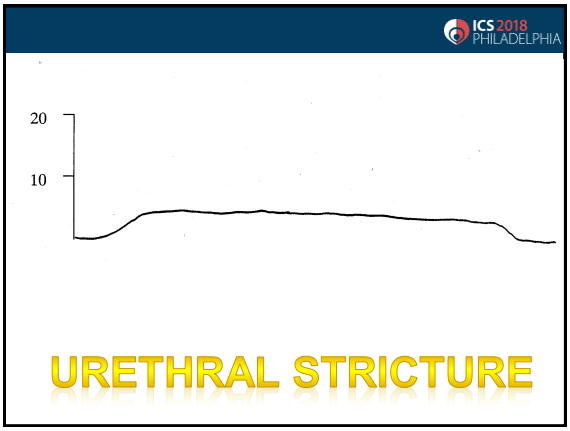
	Age	Qmax
Men	<40 yrs	>22
	40-60	>18
	>60	>13
Women	<50	>25
	>50	>18
Child	<10	>15
	10-20	>20

2SD from the mean is 10ml/s at 150ml, 15 at 500ml

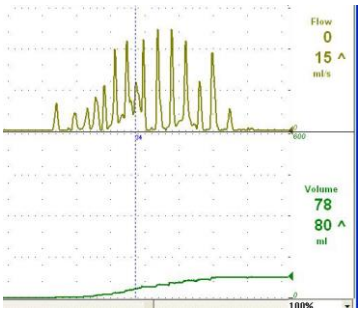
Uroflometry - Normal

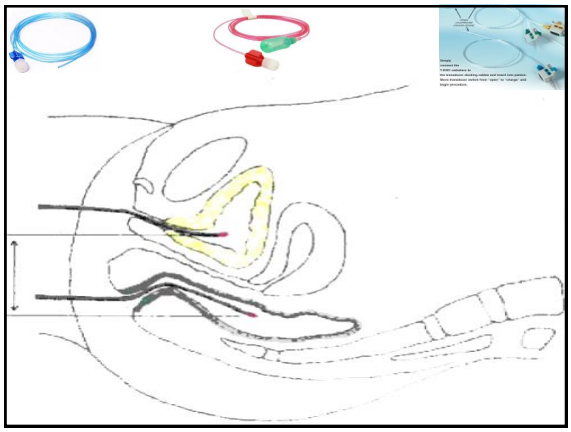






Uroflometry - Straining



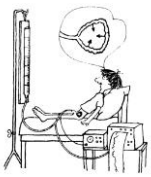


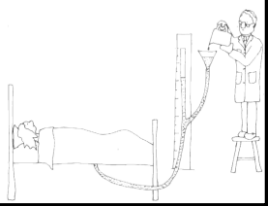
Solution infused

Saline solution or contrast

Temperature

- Room temperature





Bladder filling sensation (eo)

Is a subjective parameter

Normal bladder sensation (rule of thumb)		of capacity
• First sensation	175-250mL	33%
• First desire to void	272-450mL	66%
• Strong desire to void	429-700mL	100%

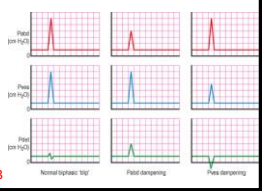
Detrusor function

$$P_{det} = P_{ves} - P_{abd}$$

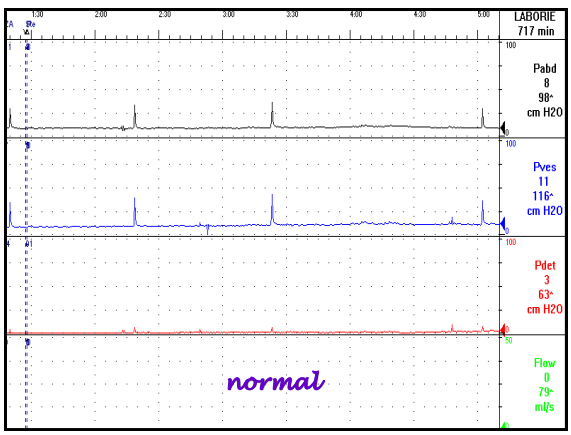
Normal detrusor function – little or no changes in pressure

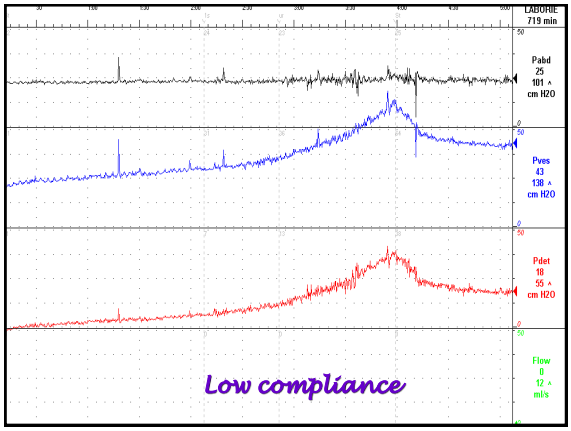
Detrusor overactivity – ANY amplitude of detrusor pressure raise before permission to void:

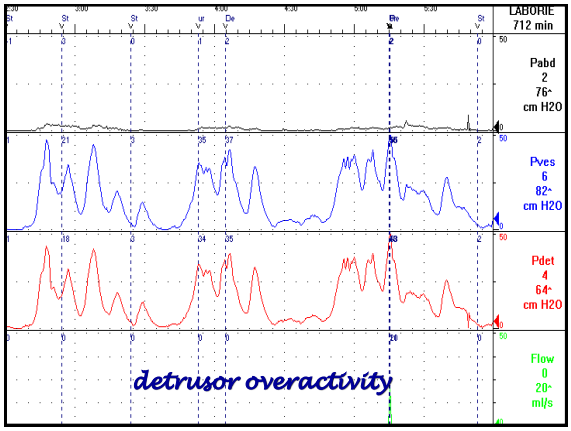
- Neurogenic
- Idiopathic

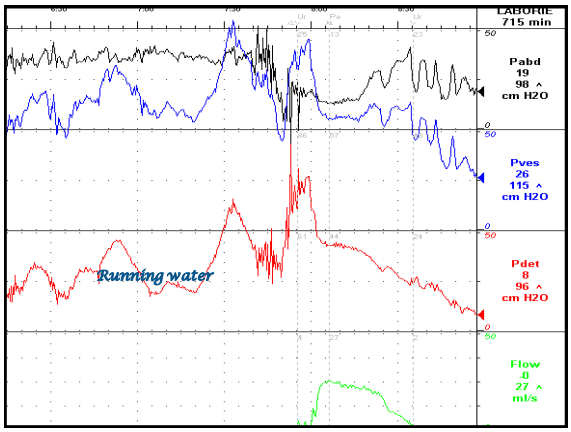


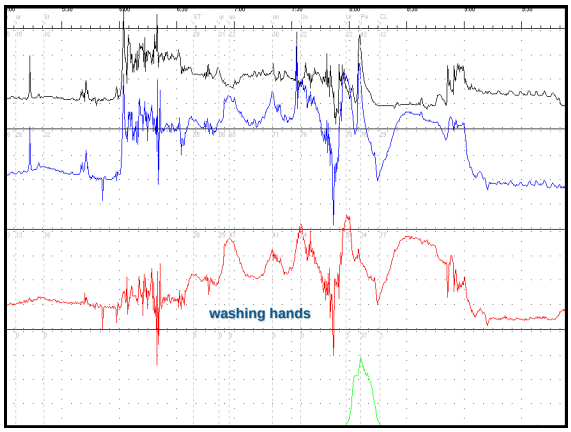
Abrams P. Urology 2003

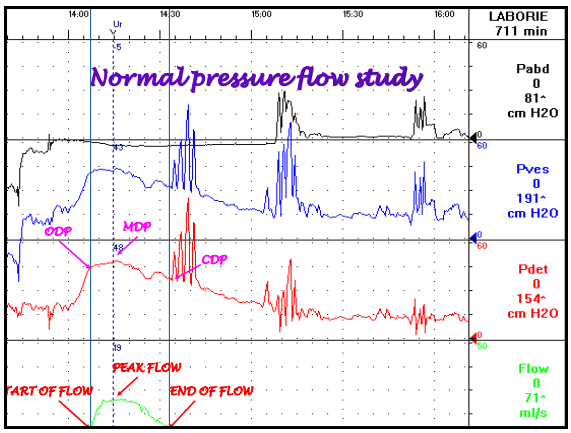


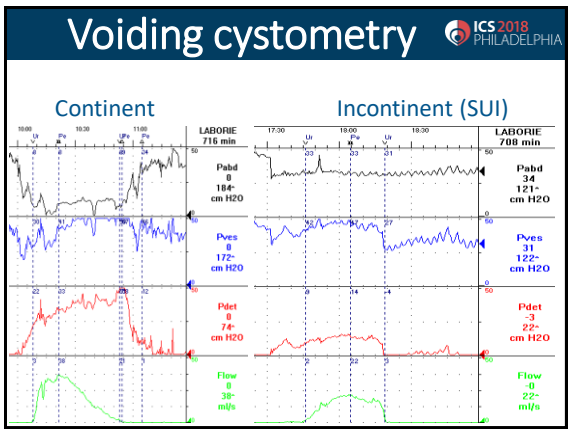

LABORIE
719 min
Pabd
25
101
cm H2O
Pves
43
138
cm H2O
Pdet
18
55
cm H2O
Flow
0
12
ml/s
Low compliance


LABORIE
712 min
Pabd
2
76
cm H2O
Pves
6
82
cm H2O
Pdet
4
64
cm H2O
Flow
0
20
ml/s
detrusor overactivity

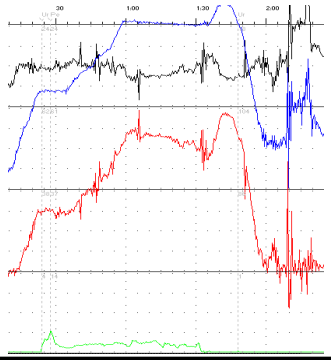

LABORIE
715 min
Pabd
19
98
cm H2O
Pves
26
115
cm H2O
Pdet
8
96
cm H2O
Flow
0
27
ml/s
Running water


washing hands

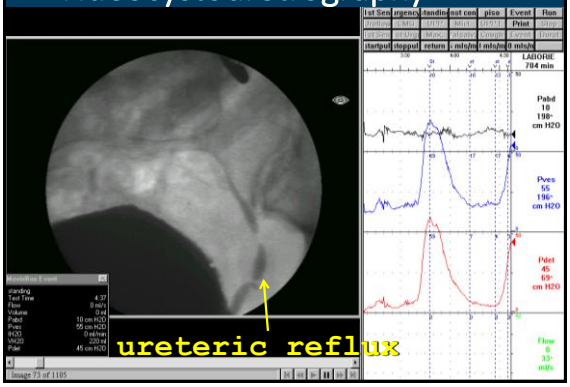

LABORIE
711 min
Normal pressure flow study
Pabd
0
81
cm H2O
Pves
0
191
cm H2O
Pdet
0
154
cm H2O
Flow
0
71
ml/s
ODP
MDP
CDP
START OF FLOW
PEAK FLOW
END OF FLOW

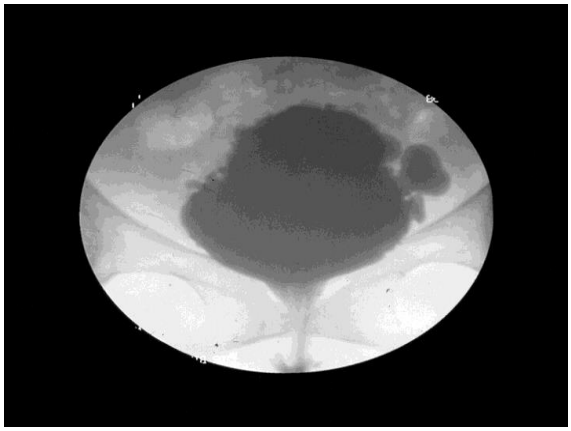

Voiding cystometry
ICS 2018 PHILADELPHIA
Continent
Incontinent (SUI)

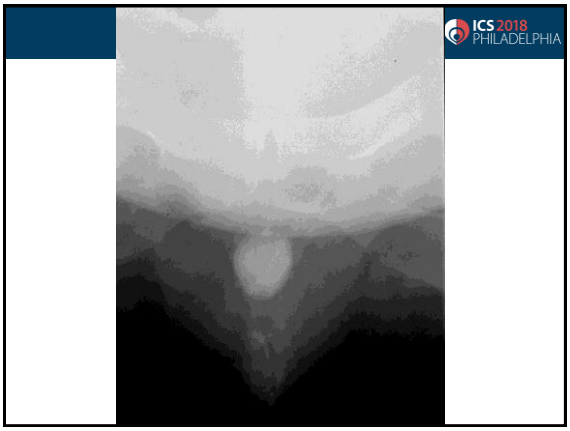
High pressure / low flow



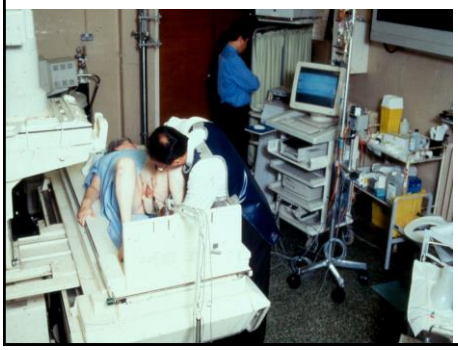
Videocystouretrography





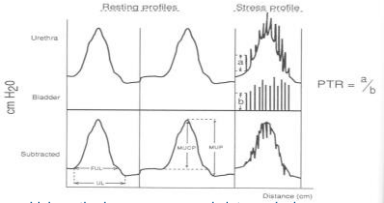


Urethral pressure profile (UPP)



Urethral pressure profile (UPP)

- Intravesical pressure measured to exclude simultaneous detrusor contraction
- Subtraction of intravesical pressure from urethral pressure produces urethral closure pressure



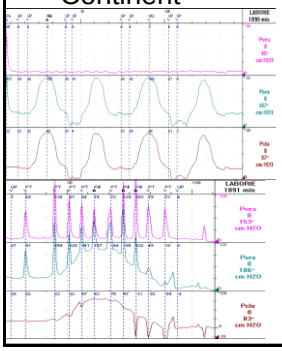
FUL = length over which urethral pressure exceeds intravesical pressure

Urethral pressure profile (UPP)

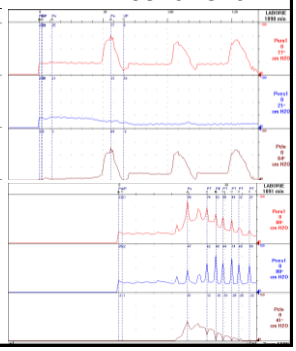
	Male		Female	
Age	Mean	Range	Mean	Range
<25	75	37-126	90	55-103
25-44	79	35-113	82	31-115
45-64	75	40-123	74	40-100
>64	71	35-105	65	35-75

UPP

Continent



Incontinent



Ambulatory urodynamics

AUM has been recognized by the ICS as a useful tool to investigate LUTS in patients with inconclusive urodynamics diagnoses (19% to 44%)

ADVANTAGES

Natural (orthograde) filling of the bladder

Less embarrassing test since the patients are fully dressed

The pressure are recorded for several hours (3-4)

The patients able to leave the urodynamic room

Increased diagnostic accuracy in the detection of DO

DISADVANTAGES

Time-consuming test

It requires trained and dedicated personnel

It requires specialized equipment

A high rate of abnormal detrusor contractions using AUM in asymptomatic controls

- **Catheter-mounted microtip transducers:**
  - silicone-covered braided metal makes them very flexible
  - low stiffness and the circumferential configuration
  - allow greater patient's mobility
  - low incidence of artifacts (eo)
- **Fluid-filled catheters:** possible but use not yet proven
- **Air - charged catheters:** possible but use not yet proven

Recording systems

Gaeltec Device

- **Goby, Laborie Medical or Luna, MMS:**
  - Newer systems
  - Small remote control attachment to capture data
  - Compatible with water, air and microtip catheters

ICS Educational Module

Instructions to the patient

ICS Educational Module 48

Recommendations

- AUM is most sensitive for the detection or exclusion of detrusor overactivity compared to laboratory cystometry (LE 2a16)
- AUM is valuable when all other diagnostic tests have failed to detect the underlying cause of LUTS and/or LUTS do not correlate to laboratory cystometry diagnosis (LE 2a)
- Stress urinary incontinence is better detected by laboratory cystometry than AUM (15) (LE1B)
- UTI must be excluded prior to commencing the test

Scientific Evidence

- Although there is no scientific evidence supporting the use of routine bowel evacuation agents before AUM test (as they can cause rectal activity and/or abdominal discomfort) an impacted bowel should be avoided
- To date there is no clear LE about AUM role in the assessment of neurogenic LUTS
- No scientific evidence demonstrating that routine antibiotic cover before and after the test is needed
- Post procedure broad spectrum antibiotic cover may be considered in patients with:
  - Diabetes
  - Recurrent urinary tract infections
  - High post micturition residual eo

ICS 2018 PHILADELPHIA

RADIOLOGIOCAL IMAGING

Imperial College Healthcare NHS NHS Trust

Ultrasound in urogynaecology

ICS 2018 PHILADELPHIA

It has become an increasingly frequent adjunct investigation in urogynecology and female urology both in the office and in the urodynamic laboratory.

Different modalities:

Perineal: Curved array probe applied to the perineum. This term incorporates transperineal and translabial ultrasound.

Introital: Sector probe applied to the vaginal introitus.

Transvaginal (T-V): Intravaginal curvilinear, linear array or sector scanning.

Transabdominal (T-A): Curvilinear scanning applied to the abdomen.

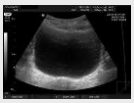
Imperial College Healthcare NHS NHS Trust

Clinical applications

ICS 2018 PHILADELPHIA

- **Bladder neck descent/mobility:** The position of the bladder neck at rest and on Valsalva.
- **Urethral funnelling:** i.e., opening of the proximal third of the urethra during coughing or on Valsalva.
- **Post void residual:** Several formulas have been described in the literature to measure the bladder volume by ultrasound. An early formula [(h × d × w) × 0.7] has been demonstrated to give reproducible results with a percentage error of 21%
- **Bladder abnormalities**: tumor, foreign body.
- **Urethral abnormality**: diverticulum.
- **Postoperative findings:** bladder neck position and mobility, position of meshes, tapes, or implants.
- **Descent of pelvic organs:** visualization of descent of the bladder, uterine cervix, and rectum during coughing or on Valsalva.
- Assessment of **voluntary pelvic floor muscle contractility**.
- **Pelvic floor/levator ani muscle defect** ("avulsion") and **hiatal ballooning**.
- Ultrasound measurements of **bladder and detrusor wall thickness**, and ultrasound **estimated bladder weight** (UEBW) are potential noninvasive clinical tools for assessing the lower urinary tract. UEBW is higher in women with overactive bladder and detrusor overactivity.

PVR measurement by US



Ultrasound bladder volume estimation can be performed in two ways:

1. By a real-time ultrasound to directly visualize the bladder.

   Griffiths CJ, et al. J Urol 1986;136:808-812

2. By using a portable bladder scanner to calculate the volume automatically without directly visualizing the bladder.

   Hartnell GG et al, Br J Radiol 60 (1987), pp. 1063–1065

PVR measurement

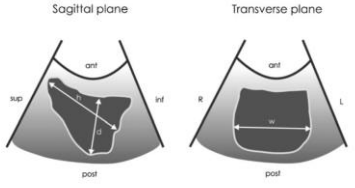
Bladder scanner advantages:

1. easy to use;
2. requires only basic training;
3. can be carried out on the ward.

Reliability? (Better with additional real-time pre-scan imaging?)

Park YH: Neurourol Urodyn 2011; 30:335–8.

Fig. 15 Ultrasound measurement of the bladder volume *from* Poston GJ et al. 1983 [33] (redrawn)



PVR

- *Threshold values delineating what constitutes an abnormal PVR are poorly defined.*
- *Most urologists agree that volumes of 50-100 mL constitute the lower threshold to define an abnormal PVR.*

Abrams PH et al . Br Med J 1978; 2: 1258

Significance of PVR
PVR and Chronic kidney disease (CKD)

- A PVR >100 mL has been associated with CKD, even if other studies do not suggest this association.
- Very large PVRs (>300 mL) may be associated with an increased risk of upper urinary tract dilation and renal insufficiency.

Kelly CE. Rev Urol. 2004;6 Suppl 1:S32-7.

Significance of PVR
PVR and Female incontinence

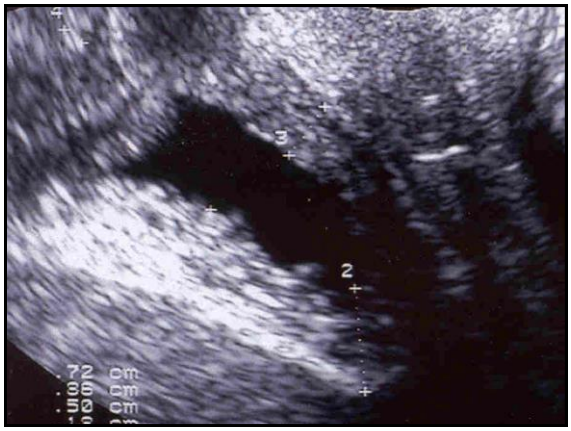
Measurement of PVR is recommended in the management of female urinary incontinence (LE 3).

Thüroff JW, et al. EAU guidelines on urinary incontinence. Eur Urol. 2011 Mar;59(3):387-400.

PVR may be useful during the assessment of women complaining of overactive bladder symptoms to exclude voiding dysfunction and anticholinergic medication should be used if PVR is low.

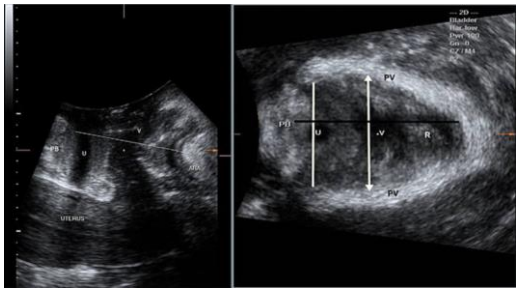
Milleman M, et al. J Urol. 2004 Nov;172(5 Pt 1):1911-4

Assessment of PVR is considered mandatory in a variety of pediatric patients such as those with voiding LUTS, UTIs, vesicoureteral reflux, posterior urethral valves or neural tube defects (LE 3).



3D ultrasound imaging of the levator ani

ICS 2018 PHILADELPHIA



3D ultrasound imaging of ballooning of the genital hiatus

ICS 2018 PHILADELPHIA

The excessive distensibility of the levator hiatus on Valsalva manoeuvre has also been associated to the severity of urogenital prolapse. An area of more than 25 cm^2, 30 cm^2, 35 cm^2,40 cm^2 has been defined as mild, moderate, marked & severe ballooning

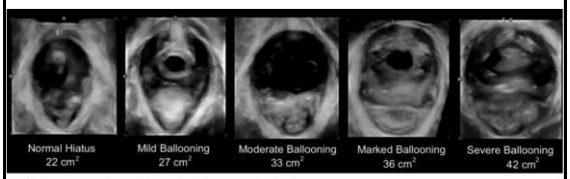


Fig. 21 *(above)*: Ballooning of the genital hiatus on Valsalva manoeuvre – levator defect

3D ultrasound imaging of the female urethra

ICS 2018 PHILADELPHIA

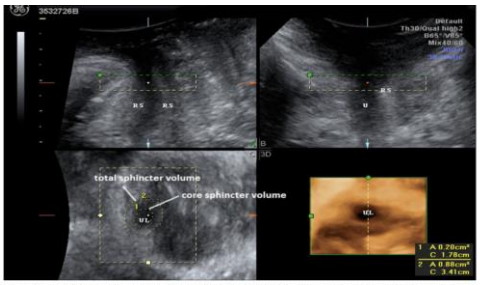
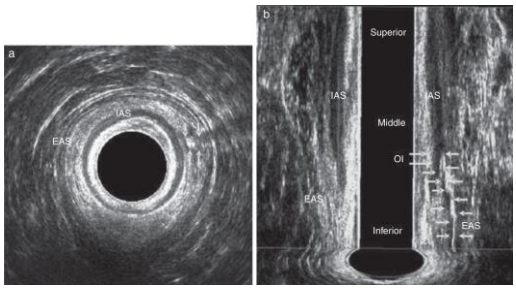


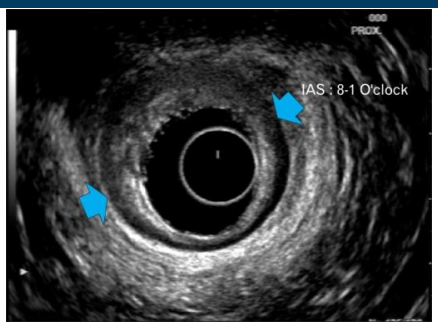
Fig. 19 *(above)*: 3D translabial image of the female urethra. The urethra lumen is shown clearly in the rendered volume image (bottom right). (*U* urethra, *UL* urethra lumen, *RS* rhabdosphincter)

Endoanal ultrasound

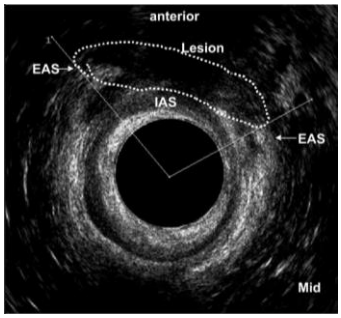
ICS 2018 PHILADELPHIA

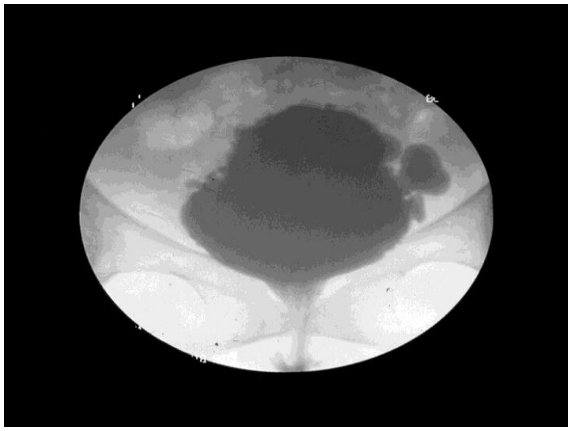


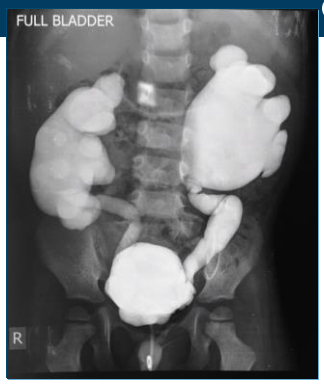
ICS 2018 PHILADELPHIA

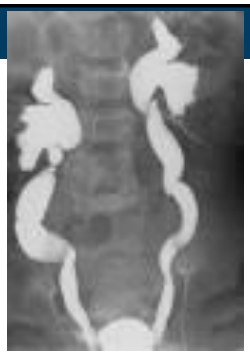


ICS 2018 PHILADELPHIA

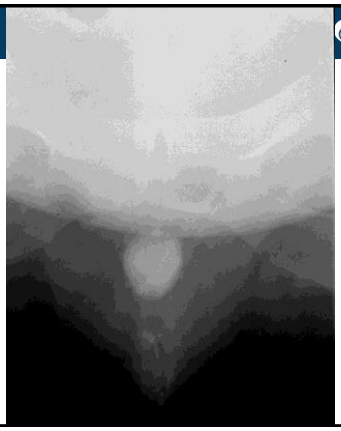






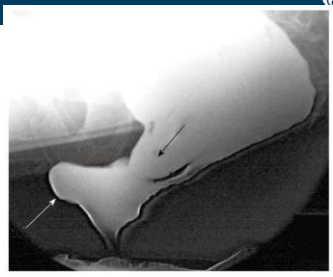


BILATERAL URETERIC REFLUX

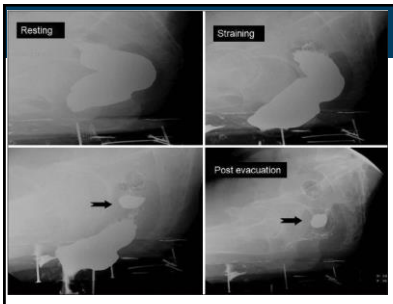


Materials required for defecography:
- barium sulfate (arrow)
- rectal insufflation syringe and tube (curved arrow)
- commode on foot end of table (black arrowhead)

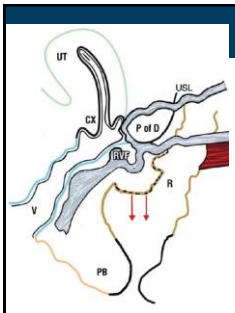
DEFECOGRAPHY

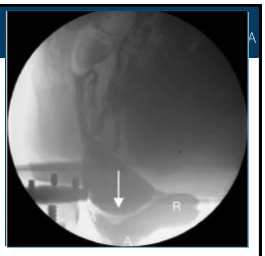


DEFECOGRAPHY
ANTERIOR RECTOCELE



DEFECOGRAPHY SIGMOID DIVERTICULAE





DEFECOGRAPHY: INTUSUSCEPTION

inwards prolapse of the rectal wall (R)

Ultrasound with kidney stone | KUB X-ray with ureteric stone | IVU – the contrast outlines drainage of kidneys | Non-contrast CT scan – offers the best resolution for detection.

KIDNEY STONES

Abscess following TVT

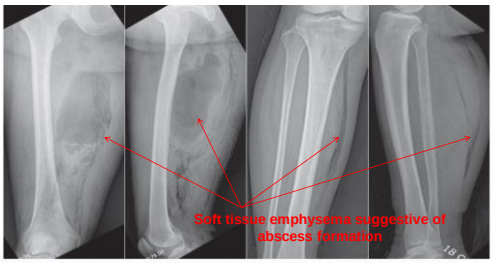
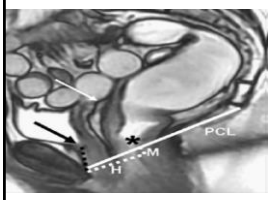


Fig. 1. Plain radiographs of right leg. Right femur anteroposterior (A) and lateral (B) radiographs show extensive soft tissue emphysema in the right posteromedial thigh and lower pelvic area, with deep-seated air-filled cystic lesion suggestive of abscess formation. The radiographs of lower leg (C, D) show the soft tissue emphysema extending inferiorly to lower calf.

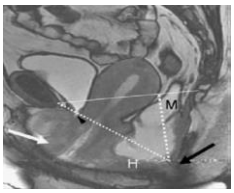
MRI

Normal



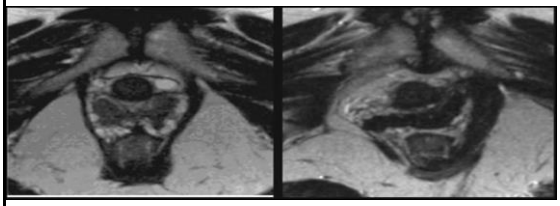
Sagittal MRI image of the pelvic floor obtained at rest in a 50-year-old normal volunteer woman. The H line is drawn from the inferior border of the pubic symphysis to the posterior wall of the rectum at the level of the anorectal junction.
The M line is drawn perpendicularly from the PCL to the most posterior aspect of the H line. *(PCL: pubococcygeal line, black arrow: bladder base, white arrow: vaginal vault, *: anorectal junction)*

Prolapse



Severe uterine prolapse in a 41-year-old woman. Sagittal function MRI image obtained during defaecation shows the uterus moving downward inside the vagina and the cervix exits the vaginal introitus (white arrow). H and M lines are abnormally elongated. Urethral funnelling without hypermobility (arrowhead) and severe posterior compartment descent (black arrow) are also noted

MRI – LAM injury



Unilateral levator defect of the pubococcygeus muscle seen on MRI imaging.

CT – LAM

ICS 2018 PHILADELPHIA

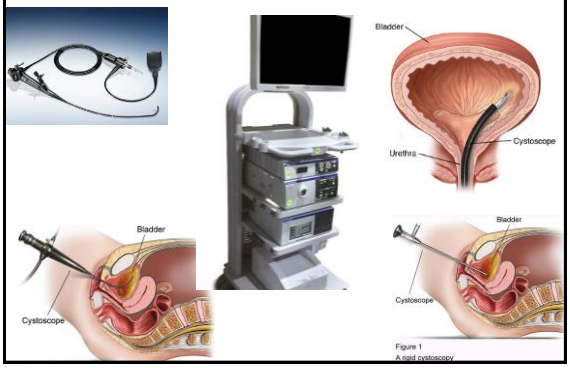
CT is not routinely recommended for imaging the pelvic floor mainly due to irradiation and poor soft tissue contrast.

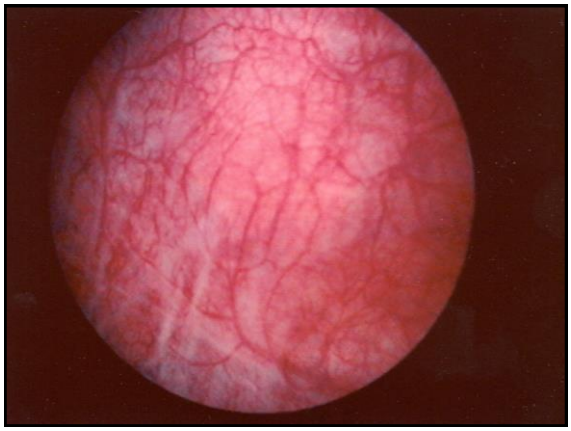
A multiplanar spiral CT offers an accurate visualization of the pelvic floor soft and bony structures by reconstruction of axial images using 1 mm thick slices without gaps thus increasing the diagnostic accuracy of pelvic floor anatomical disorders (ie. LAM trauma)

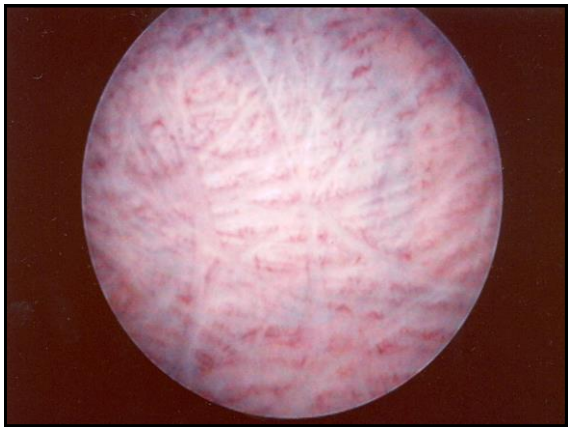
Computed tomography (CT) of the LAM. Axial view of CT multiplanar 3-dimensional data volume, with 1 mm slice thickness without gaps, showing an intact pubovisceral muscle arising from the body of the pubic bone and forming a sling around the rectum (U: urethra, V: vagina, R: rectum, PM: pubovisceral muscle, PR: puborectalis muscle).

Cystoscopy

Imperial College Healthcare NHS Trust

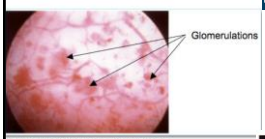






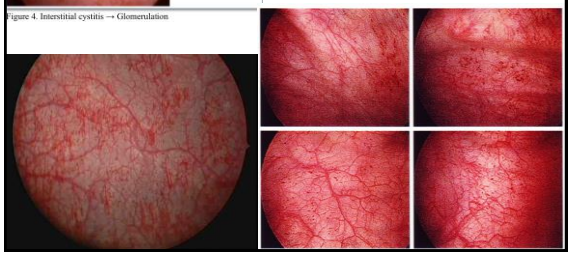
Cystoscopy

Imperial College Healthcare NHS Trust



Glomerulations

Figure 4. Interstitial cystitis → Glomerulation



Cystoscopy

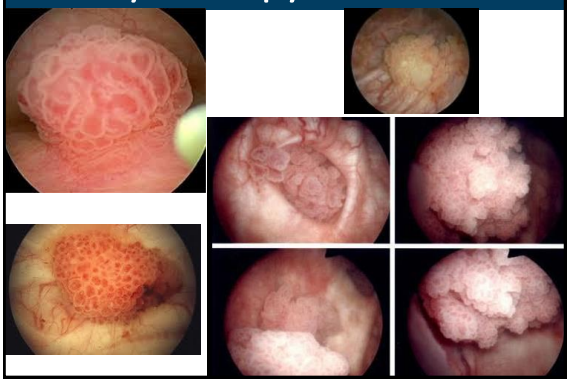
Imperial College Healthcare NHS Trust

Hunner's lesion

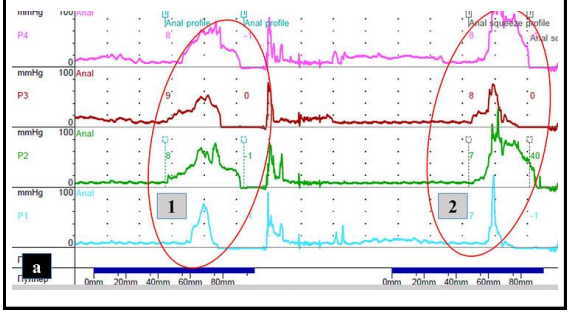
A reddened mucosal area with small vessels radiating towards a central scar, with a fibrin deposit or coagulum attached to this area.

This site ruptures with increasing bladder distension, with petechial oozing of blood from the lesion.

Cystoscopy



Anorectal manometry



NEUROPHYSIOLOGIC TESTS

1. EMG
2. Nerve conduction studies
3. Spinal reflex testing
4. Anal manometry
5. MRI (lumbar and pelvic)
6. Dynamic proctography
7. Endo-anal ultrasound

Imperial College Healthcare NHS Trust

Neurophysiologic testing

1. Pelvic floor disorder in a patient with known neurologic disease (i.e., multiple sclerosis, Parkinson's disease)
2. Voiding dysfunction in young women
3. Urinary retention in patient without obvious cause (i.e., advanced POP, previous continence surgery)
5. Anal incontinence
6. Prior to anal sphincter repair (for prognosis and sphincter mapping)
7. Unexplained perineal numbness or pain

Imperial College Healthcare NHS Trust

ELECTROMYOGRAPHY

- Method of studying electrical activity of muscle
- Electrodes are inserted into or placed on the surface of a muscle
- Bioelectric potentials generated by the depolarization of the skeletal striated muscle are:
  - Recorded
  - Filtered
  - Amplified
  - Displayed on an oscilloscope for visual analysis

Imperial College Healthcare NHS Trust

NEEDLE ELECTRODES

Advantages: Consistently more interpretable than surface electrodes

Disadvantage:
1.difficulties associated with correct needle placement
2.patient discomfort
3.limited patient mobility during testing

SURFACE ELECTRODES

Advantages: Simple, non invasive

Disadvantage: Prone to artifacts/contamination from signal from other muscles

In view of the above surface electrodes more often used

Anal Sphincter

- Needle inserted 1cm outside the anal orifice to a depth of:
  - 3–6 mm (subcutaneous portion of the EAS)
  - 1–3 cm (deep portion of the EAS)
- At least **4 quadrants**, divided into the upper and lower and left and right portions of EAS
- At least **20 MUAPs** should be recorded to adequately evaluate the EAS

Urethral Sphincter

- Needle inserted 5 mm anterior to the external urethral meatus (12:00 position) to a depth of 1–2 cm (**periurethral approach**)
- Needle inserted 2 cm proximal to the external urethral meatus, off the midline, directed laterally into the urethral sphincter. (**transvaginal approach**)
- Although slightly more painful, periurethral approach provides superior sampling of the urethral sphincter, obtaining as many as twice the number of MUAPs as the transvaginal approach
- At least **10 MUAPs** should be recorded to adequately evaluate the urethra

Levator Ani Muscle

- Transvaginal approach
- The muscles localized by first inserting two fingers into the vagina and asking the patient to contract
- The electrode is inserted using the opposite hand in at least two sites on the muscle
- This is then repeated on the opposite side
- **No standardized location for needle insertion** but the ischial spine can be used as a fixed reference point

ELECTROMYOGRAPHY

EMG studies used to evaluate pelvic floor disorders can be separated into two categories

1. Kinesiological EMG (kEMG)

to assess the activity or inactivity of a muscle

usually the urethral or anal sphincter

used with urodynamics and anal manometry to assess sphincter relaxation during voiding or defecation

used for biofeedback during pelvic muscle rehabilitation for UI or FI

2. Motor-unit EMG

a diagnostic test used to assess the neuromuscular function of a muscle.

It can differentiate normal muscle from denervated/reinnervated or myopathic muscle.

Common techniques used for motor-unit EMG are:

1. concentric needle EMG (CnEMG)
2. single-fiber EMG (SfEMG).

NERVE CONDUCTION STUDIES

- Nerve injury affects the rate at which a impulse travels

Demyelinating injury → resistance increases → conduction velocity decreases

1. **Pudendal nerve terminal motor latency (PNTML)**
   prolonged if greater than 2.4 msec
2. **Perineal nerve terminal motor latency (PeNTML)**
   prolonged if greater than 2.6 msec

Latency: time for an applied stimulus to generate a motor or sensory response over a set distance

3. **Compound motor action potential (CMAP):**
   contraction of a muscle in response to an electrical stimulus

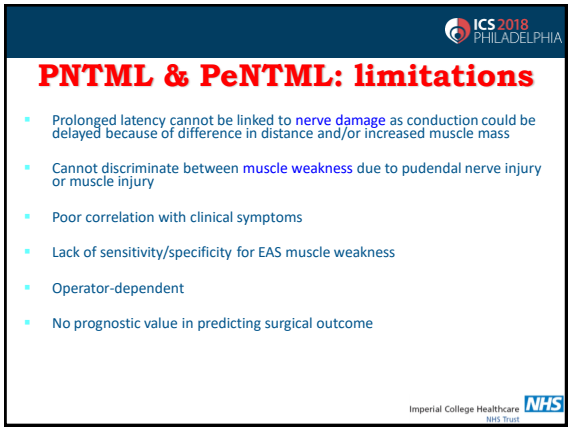
St. Mark's disposable electrode for PNTML & PeNTML

Electrodes fitted over the index finger of a disposable glove at the level of ischial spine.

Stimulating electrode positioned at the fingertip at level of EAS

Recording electrode positioned at the base of the index finger

Transrectal or transvaginal


ICS 2018 PHILADELPHIA
PNTML & PeNTML: limitations
Prolonged latency cannot be linked to nerve damage as conduction could be delayed because of difference in distance and/or increased muscle mass
Cannot discriminate between muscle weakness due to pudendal nerve injury or muscle injury
Poor correlation with clinical symptoms
Lack of sensitivity/specificity for EAS muscle weakness
Operator-dependent
No prognostic value in predicting surgical outcome
Imperial College Healthcare NHS Trust

OAB
Ambulatory Management

Dudley Robinson MD FRCOG
Department of Urogynaecology
King's College Hospital, London

Disclosures

Research
Astellas, Allergan, Ixaltis
Consultancy
Astellas, Ferring, Allergan, Ixaltis
Speaker
Astellas, Pfizer, Contura, Ferring

Overactive Bladder

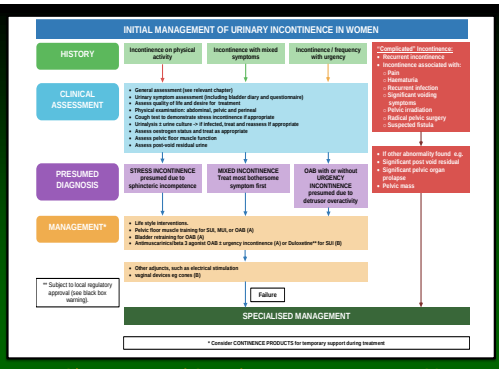
'Urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathology'

Haylen et al, 2010

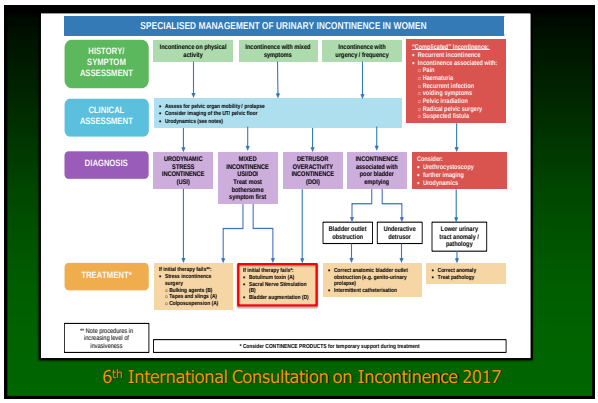
Prevalence of OAB

A prevalent condition	16.6% of the population in Europe aged 40 years and over suffer from OAB symptoms[1]
Under-diagnosed	Most sufferers in Europe do not seek medical attention or remain undiagnosed[2]
Undertreated	In Europe, only 27% of those with OAB who consult a doctor receive treatment[1]
Increases with age	30-40% of those aged 75 years and over in Europe suffer from OAB[1]
Significant burden	OAB sufferers in the US reported 20% more physician visits and 138% more UTIs[3]

1. Milsom I, Abrams P, Cardozo L et al BJU Int 2001; 87(9):760-6
2. Goepel M, Hoffmann JA, Piro M et al Eur Urol 2002; 41(3):234-9
3. Wagner TH, Hu TW, Bentkover J et al Am J Manag Care 2002; 8: S598-607



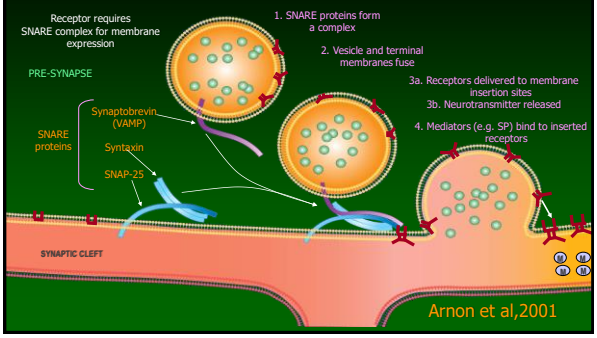
6th International Consultation on Incontinence 2017



6th International Consultation on Incontinence 2017

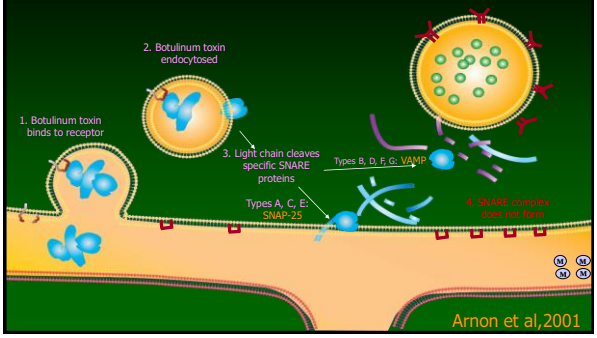
OAB: Botulinum Toxin

Mechanism of Action: Neurotransmitter release



Arnon et al,2001

Mechanism of Action: Botulinum Toxin



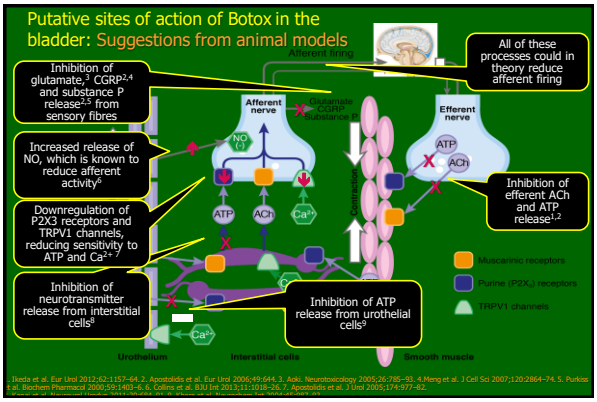
Arnon et al,2001

Botox: Motor and sensory mechanisms of action

- Botox is thought to have a recognised targeted, sensorimotor action

Motor	Sensory
Botox blocks peripheral acetylcholine release at presynaptic cholinergic nerve terminals Botox affects the efferent pathways of detrusor activity via inhibition of acetylcholine release	Botox blocks the release of neurotransmitters associated with the genesis of pain Botox suppresses peripheral sensitisation, thereby possibly also inhibiting central sensitisation Botox may inhibit afferent neurotransmitters and sensory pathways

Putative sites of action of Botox in the bladder: Suggestions from animal models



Jiseda et al. Eur Urol 2013;62:1157–64. 2. Apostolidis et al. Eur Urol 2006;49:644. 3. Aoki. Neurotoxicology 2005;26:785–93. 4.Meng et al. J Cell Sci 2007;120:2864–74. 5. Purkiss et al. Biochem Pharmacol 2000;59:1403–6. 6. Collins et al. BJU Int 2013;11:1018–26. 7. Apostolidis et al. J Urol 2005;174:977–82.

Evidence supporting the sensory and motor action of Botox in OAB

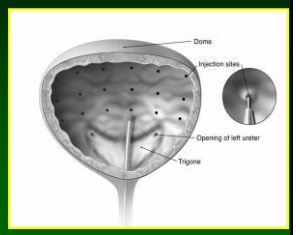
Motor	Sensory
Urodynamic evidence showed a decrease in phasic involuntary contractions after Botox treatment[1–3]	Patients reported a rapid reduction (within 3 weeks) in sensations of urgency after Botox treatment[4,5]
Treatment with Botox increased bladder capacity[6]	Urgency severity was reduced in patients treated with Botox[7]
Improved urinary continence via Botox action on motor neurones[8]	In neural and bladder tissue, Botox modulated the release of sensory transmitters[9]
In bladder tissue, Botox modulated the release of acetylcholine[10]	Botox reduced levels of sensory receptors in bladder tissue, and decreased ATP release and increased NO release from the bladder wall[11,12]

1. Reitz et al. Eur Urol 2004;45:510–5. 2. Schurch et al. J Urol 2005;174:196–200. 3. Popat et al. J Urol 2005;174:984–8. 4. Rapp et al. Urology. 2004;63:1071–107. 5. Schmid et al. J Urol 2006;176:177–85. 6. Kuo. Neurourol Urodyn. 2011;30:1497–502. 7. Sievert et al. EAU 2014. Poster 577. 8. Cruz. Urology 2004;63(3 Suppl 1):65–73. 9. Apostolidis et al. Eur Urol 2006;49:644–50. 10. MacKenzie et al. Neuroscience 982;7:997–1006. 11. Apostolidis et al. J Urol 2005;174:977–83. 12. Collins et al. BJU Int 2013;11:1018–26.

Botox: Ambulatory Method

Technique

- Rigid or flexible cystoscope
- LA
- 20 Intradetrusor injections
- Sparing trigone



Dosage

- OAB – 100 units
- NDO – 200 units

Botulinum Toxin: EMBARK

- Prospective, multicentre double blind randomised placebo controlled trial
- 64 sites within Europe and USA
- 548 patients with OAB: Botox 100iu or Placebo
- Greater reduction in UI episodes with Botox
  Botox: -2.95 vs Placebo: -1.03; p<0.001
- Significant reduction in frequency, urgency, nocturia
- Significant improvement in QoL and PROMs
- Higher PVR in Botox group: (46.9 mls vs 10.1mls)
- Higher CISC in Botox group: (6.9% vs 0.7%)
- Higher rates of UTI with Botox: (24.1% vs 9.6%)

EMBARK

Chapple et al, 2013

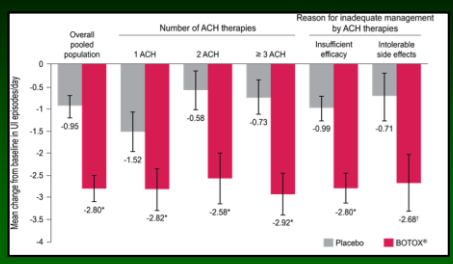
Antimuscarinic or Botulinum Toxin?

- Multicentre double blind randomised placebo controlled trial
  Antimuscarinic vs Botulinum Toxin 100iu vs placebo
- 249 women with UUI; 6 mths duration
- Mean reduction in UUI episodes per day
  Antimuscarinic: 3.4 Botulinum Toxin: 3.3
- Complete resolution
  Antimuscarinic: 13% Botulinum Toxin: 27%
- Antimuscarinics associated with similar QoL but
  Higher dry mouth (46% vs 31%; p=0.02)
  Lower catheter use (0% vs 5%; p=0.01)
  Lower UTI (13% vs 33%; p=0.001)

Visco et al, 2012

Refractory OAB: Botulinum Toxin

Mean change from baseline in UI episodes/day at Week 12



Baseline daily UI episodes

Placebo (n = 548): 5.4 ± 3.6 BOTOX® (n = 557): 5.5 ± 3.7

Sievert et al 2014

Refractory OAB: ROSETTA Trial

- Prospective randomised trial of refractory OAB
- 386 women; 6 month follow up
- Botulinum Toxin 200 u Vs Sacral Neuromodulation
- Greater reduction in UUI with botulinum toxin (p=0.001)
- Dry rates: Botulinum Toxin: 20% SNS: 4%
- UTI higher with Botulinum Toxin (35% vs 11%; p<0.001)
- CISC rate in Botulinum toxin: 8% at 1 mth, 2% at 6 mths
- SNS – 3% Explanation at 6 mths
- Greater improvement and patient satisfaction with Botulinum Toxin
- No significant difference in PGII

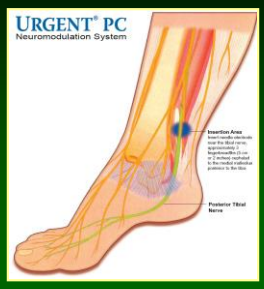
Amundsen et al, 2016

Refractory OAB: ROSETTA Trial

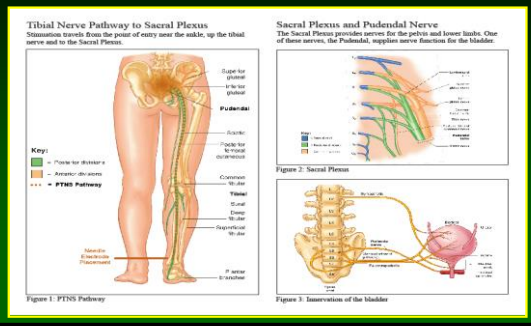
- Prospective 24 month multicentre randomised study of:
  194 SNS patients and 192 Botulinum Toxin patients
- No difference in reduction of UUI episodes
  -3.88 vs -3.50 (95%CI: 0.14-0.89; p=0.15)
- Higher UUI resolution with Botulinum toxin at 6 mths
- No difference in UUI resolution at 24 mths
- Higher satisfaction rates with Botulinum Toxin
- Recurrent UTI higher with Botulinum Toxin:(24% vs 10%)
- Botulinum Toxin: CISC 6%
- SNS: Revision 3% Explantation: 9%

Amundsen et al, 2018

Overactive Bladder: PTNS



PTNS: Mode of Action



PTNS: Mode of Action

- Posterior tibial nerve is mixed motor and sensory nerve
- Modulates signals to and from bladder via sacral plexus

Vandoninck et al 2003

- Carry-over effect for pudendal nerve and intravesical stimulation
- Caused by negative modulation of excitatory synapses of micturition reflex

Jiang et al 1998

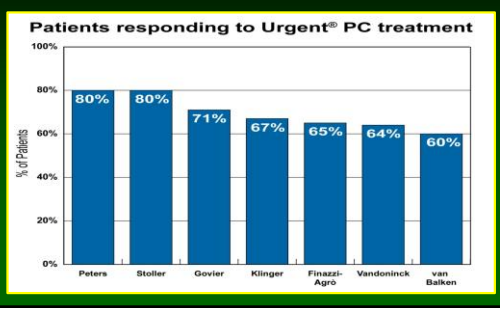
- Prolonged decrease of synaptic efficacy due to intense activation of excitatory synapses causes long term suppression

Bear & Malenka 1994

- Modulatory effect prolonged by repeated stimulation since carry-over effect is reversible

Jiang et al 1998

PTNS: Response Rate



PTNS: SUmiT Trial

- Randomised double blind trial of PTNS vs Sham in OAB
- 220 patients; 13 week follow up

	PTNS Responders	Sham Responders	p-value
OAB symptoms *(intent-to-treat)*	60/110 (54.5%)	23/110 (20.9%)	<0.001
Overall bladder symptoms	60/103 (58.3%)	23/105 (21.9%)	<0.001
Urgency	44/103 (42.7%)	24/105 (22.9%)	0.003
Frequency	49/103 (47.6%)	23/105 (21.9%)	<0.001
Urge incontinence	39/103 (37.9%)	23/104 (22.1%)	0.02

Peters et al, 2010

PTNS: OrBIT Trial

- Randomised Trial of PTNS Vs Tolterodine ER in OAB
- 100 patients; 12 week follow up

Patient Global Response Assessment (GRA) at 12 weeks

	PTNS	Tolterodine ER
Cured	1/44 (2.3%)	2/42 (4.8%)
Improved	34/44 (77.3%)	21/42 (50.0%)
No improvement/worsening	9/44 (20.5%)	19/42 (45.2%)
Cured or Improved*	35/44 (79.5%)	23/42 (54.8%)

*p = 0.01

Peters et al, 2009

OAB: PTNS vs Medication

- Prospective crossover trial in 40 women
  PTNS vs Solifenacin
- Significant reduction in frequency, nocturia and UUI
- Greater reduction in urgency with PTNS
- Greater improvement in HRQoL

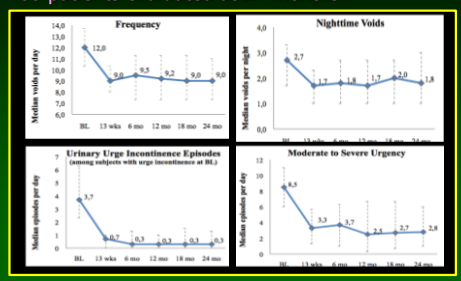
Vecchioli-Scaldazza et al 2013

- Prospective randomised trial of 36 women over 3 months
  PTNS vs Tolterodine 2mg bd
- Significant reduction in in UUI episodes in both groups
- No difference between groups; Fewer adverse effects with PTNS

Preyer et al 2015

PTNS: STEP - Long Term Efficacy

- 35 patients evaluated at 24 months



Peters et al, 2012

PTNS: Systematic Review

- To evaluate the effectiveness of PTNS in OAB
- Initial success rates: 37-82%
- 4 Randomised controlled trials favoured PTNS over sham
  RR 7.02; 95%CI 1.69-29.17
- 2 Randomised controlled trials found no difference with antimuscarinic therapy
- Pooled subjective success rates: 61.4%; 95% CI: 57.5-71.8
- Pooled objective success rate: 60.6%; 95% CI: 49.2-74.7

Burton et al 2012

Refractory OAB: PTNS or Botox?

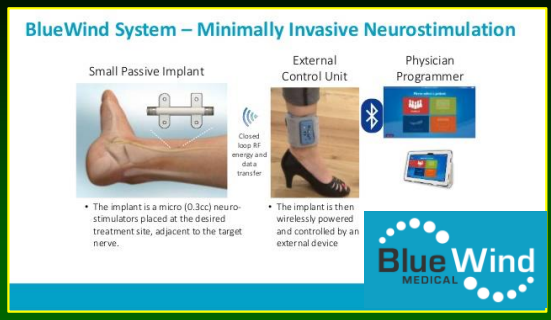
- Prospective randomised trial of 60 patients with refractory idiopathic OAB
  PTNS vs Botulinum Toxin 100u
- Significant improvement with Botox at 9 mths in:
  OAB –SS Urgency Score HRQoL UDS
- Initial significant improvement in the PTNS arm in all outcome measures but not sustained at 9 mths
- Botox: CISC: 6.6% UTI: 6.6%
- PTNS: Local minor adverse effects – pain and bleeding

Sherif et al, 2017

PTNS: Bluewind Implant

- Prospective 6 month multicentre study in 36 patients with OAB
- Bluewind Renova Implantable tibial nerve system
- 71% success at 6 mths; Dry rate: 27.6%
- Significant reduction in IEF, severity and pad usage
- Significant improvement in HRQoL
- Adverse events;
  - Implant site pain: 13.9%
  - Suspected infection: 22.2%
  - Procedural wound complications: 8.3%

Heesakkers et al 2018



Conclusions: Ambulatory Management of OAB

- Conservative therapy is indicated as primary treatment
- May be combined with pharmacotherapy in patients with persistent symptoms
- Refractory OAB may be managed in the ambulatory clinic

Botulinum Toxin

- Effective and well tolerated under local anaesthetic using a flexible cystoscope

Percutaneous Tibial Nerve Stimulation

- Similar efficacy to drug therapy and well tolerated
- May be considered before more invasive therapy such as sacral neuromodulation

IRCCS Ospedale San Raffaele Milano
Università Vita-Salute San Raffaele
Italy

Ambulatory management of GSM

Prof Stefano Salvatore

DISCLOSURES

- Speaker fee from DEKA
- Research grants from DEKA
- Speaker fee from Pierre Fabre
- Speaker fee from Astellas
- Speaker fee from Shionogi

DEFINITION

ISSWSH MEETING

NAMS
THE NORTH AMERICAN MENOPAUSE SOCIETY

Menopause: The Journal of The North American Menopause Society
Vol. 21, No. 10, pp. 000-000
DOI: 10.1097/gme.0000000000000329

SPECIAL FEATURE

Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and The North American Menopause Society

David J. Portman, MD,[1] Margery L.S. Gass MD, NCMP,[2] on behalf of the Vulvovaginal Atrophy Terminology Consensus Conference Panel

GSM

Genitourinary syndrome of menopause: New terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and The North American Menopause Society

D.J. Portman *, M.L.S. Gass, on behalf of the Vulvovaginal Atrophy Terminology Consensus Conference Panel[1]

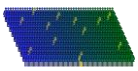
Is a chronic, progressive, vulvovaginal, sexual and lower urinary tract condiction that results from decreased estrogen

*"Genitourinary syndrome of menopause ... may include but is not limited to **genital symptoms** of dryness, burning, and irritation; **sexual symptoms** of lack of lubrication, discomfort or pain, and impaired function; and **urinary symptoms** of urgency, dysuria and recurrent UTIs."*

GSM

VULVOVAGINAL ATROPHY

The VIVA (Vaginal Health: Insights, Views & Attitudes)



- 80% considered it to negatively affect their lives
- **75% reported negative consequences on sex life**
- **68% reported that it makes them feel less sexual**
- 36% reported that it makes them feel old
- **33% reported negative consequences on marriage/ relationship**
- **26% reported a negative effect on self-esteem**
- 25% reported that it lowers QOL

1. Nappi RE, Kokot-Kierepa M. Vaginal Health: Insights, Views & Attitudes (VIVA)Vresults from an international survey. Climacteric 2012; 15:36-44.
2. Simon JA, Kokot-Kierepa M, Goldstein J, Nappi RE. Vaginal health in the United States: results from the Vaginal Health: Insights, Views & Attitudes survey [published online ahead of print April 15, 2013]. Menopause doi: 10.1097/GME.0b013e318287342d.

GSM

- During 1881-1890, the average life expectancy of a woman in Australia was **50.8 years**
- Now life expectancy is **84.3 years**. The average age for menopause is 51 years old. Women now have 30+ years to live after menopause.
- ***In 1990 there were approximately 467 million women aged ≥ 50 years throughout the world; this number is expected to have increased to 1200 million by year 2030***

Hill K, Maturitas 1996

GSM

VULVOVAGINAL ATROPHY

Menopause. 2013 Sep;20(9):888-902
Management of symptomatic vulvovaginal atrophy: 2013 position statement of The North American Menopause Society

- Guidelines for chronic therapy of atrophic vaginitis recommend use of the smallest effective **estrogen dose**
- Once urogenital function has improved, the dose of local estrogen can be tapered for long-term maintenance therapy
- Safety data from studies on local estrogen do not go beyond one year

GSM

SYSTEMIC HRT

- Suggested to patients who seek relief from GSM symptoms in addition to relief from hot flashes and protection from osteoporosis.
- The lowest effective dosage of systemic ET is always advisable

- **10–25%** of women who use HRT present the same symptoms of vaginal atrophy, thus **receiving no benefit** from the systemic therapy.
- This data, together with the concerns around HRT safety, explain why systemic therapy is not usually recommended for women who experience only vaginal-atrophy related symptoms.

GSM

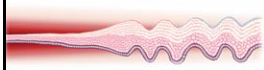
LOCAL ESTROGEN

- Most accepted form of therapy for GSM; it also offers the fastest and most effective symptomatic relief
- Advised to patients who seek relief from solely vaginal atrophy symptoms
- Low-dose vaginal estrogens decrease vaginal pH, increase the number of vaginal lactobacilli, improve vaginal and urethral cytology, and prevent frequent UTI.

- There is **poor evidence on the safety of any vaginal product after one year of use**.
- Long period treatments can provoke local inflammation and/or reduced therapeutic effect due to the drug habit.

GSM

SELECTIVE ESTROGEN RECEPTOR MODULATOR



- A therapeutic pharmacologic treatment option for patients who are not candidates for ET
- Efficacious and safe in treating vulvovaginal atrophy and dyspareunia by improving vaginal structure and pH

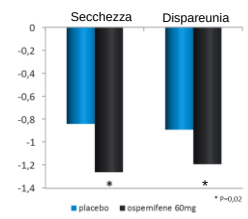
"Ospemifene remains efficacious and safe up to 52 weeks while providing greater symptomatic relief than vaginal lubricants. There were no cases of endometrial cancer and <1% of patients experienced endometrial hyperplasia with treatment."

Constantine et al., Endometrial safety of ospemifene: results of the phase 2/3 clinical development program. Menopause 2015;22:36-43.

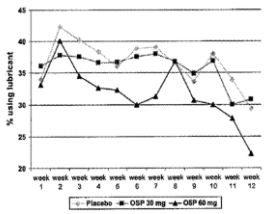
GSM

OSPEMIPHENE

MEAN CHANCE IN MBS SCORE COMPARED TO BASELINE



WEEKLY USE OF LUBRICANTS

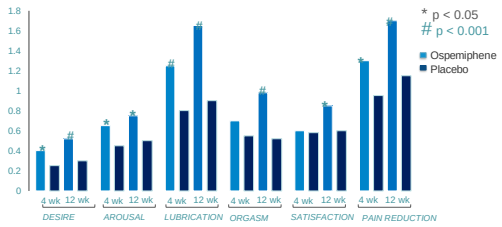


Bachmann GA, et al. Menopause 2010; 17: 480-486.

GSM

OSPEMIPHENE

Channge from baseline at 4 and 12 weeks in each single FSFI domain



Constantine G, et al. Climacteric 2015; 18: 226-232

CONCISE REVIEW FOR CLINICIANS

MAYO CLINIC

CrossMark

Genitourinary Syndrome of Menopause: Management Strategies for the Clinician

Stephanie S. Faubion, MD; Richa Sood, MD; and Ekta Kapoor, MBBS

TABLE 1. Hormonal Therapy for Management of GSM

Treatment	Product	Dosage: Initial	Dosage: Maintenance	Comments
Vaginal cream				
Estradiol-17β	Estrace	0.5–1 g daily for 2 wk	0.5–1 g 1–3 times weekly	FDA-approved dose is higher loading dose (2–4 g daily; maintenance dose, 1 g 1–3 times weekly)
Conjugated estrogens	Premarin	0.5–1 g daily for 2 wk	0.5–1 g 1–3 times weekly	FDA-approved dose is higher and administration is cyclical (for GSM: 0.5–2 g daily for 21 d and then off for 7 d; for dyspareunia: 0.5 g daily for 21 d and then off for 7 d or 0.5 g twice weekly)
Vaginal insert				
Estradiol hemihydrate	Vagifem, Yuvafem	10-μg insert once daily for 2 wk	1 twice weekly	…
Estradiol-17β softgel capsules	TX-004HR	4, 10, or 25 μg daily for 2 wk	1 twice weekly	This product is not yet FDA approved
DHEA (prasterone)	Intrarosa	6.5 mg once daily	6.5 mg once daily	…
Vaginal ring				
Estradiol-17β	Estring	Insert for 90 d (2 mg releases approximately 7.5 μg daily)	Change every 90 d	…
Estradiol acetate	Femring	Insert for 90 d (12.4 mg or 24.8 mg releases 0.05 mg or 0.1 mg daily, respectively)	Change every 90 d	This product is delivered vaginally but it provides systemic hormone levels to treat VMS and GSM
SERM				
Ospemifene	Osphena	60 mg daily	60 mg daily	FDA approved for dyspareunia

DHEA = dehydroepiandrosterone; FDA = US Food and Drug Administration; GSM = genitourinary syndrome of menopause; SERM = selective estrogen receptor modulator; VMS = vasomotor symptoms; … = no comment.

Adapted from Menopause,[1] with permission.

GSM

OSPEDALE SAN RAFFAELE

European Review for Medical and Pharmacological Sciences 2016; 20: 4190-4195

Postmenopausal vulvovaginal atrophy (VVA) is positively improved by topical hyaluronic acid application. A prospective, observational study

M. ORIGONI, C. CIMMINO, G. CARMINATI, E. IACHINI, C. STEFANI, S. GIRARDELLI, S. SALVATORE, M. CANDIANI

Department of Obstetrics and Gynecology, Vita Salute San Raffaele University School of Medicine, IRCCS, Ospedale San Raffaele, Milan, Italy

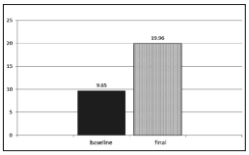


Figure 1. Vaginal Health Index (VHI) mean scores at baseline and after treatment (Wilcoxon signed-rank test: $p < 0.0001$).

GSM

OSPEDALE SAN RAFFAELE

European Review for Medical and Pharmacological Sciences 2016; 20: 4190-4195

Postmenopausal vulvovaginal atrophy (VVA) is positively improved by topical hyaluronic acid application. A prospective, observational study

M. ORIGONI, C. CIMMINO, G. CARMINATI, E. IACHINI, C. STEFANI, S. GIRARDELLI, S. SALVATORE, M. CANDIANI

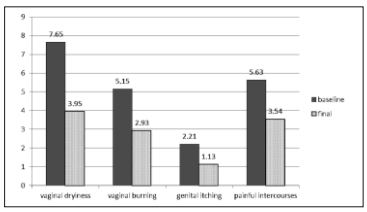


Figure 2. Visual Analogic Scale (VAS) mean scores of symptoms at baseline and after treatment (Wilcoxon signed-rank test: $p < 0.0001$).

GSM

OSPEDALE SAN RAFFAELE

ENERGY BASED DEVICES

- Radiofrequency
- LASER

GSM

OSPEDALE SAN RAFFAELE

FDA Warns Against Use of Energy-Based Devices to Perform Vaginal 'Rejuvenation' or Vaginal Cosmetic Procedures: FDA Safety Communication

Date Issued:

July 30, 2018

Audience:

- Patients considering any vaginal "rejuvenation" or cosmetic vaginal procedure, or procedures intended to treat vaginal conditions and symptoms related to menopause, urinary incontinence, or sexual function
- Health care providers who perform vaginal procedures using energy-based devices

Purpose:

To alert patients and health care providers that the use of energy-based devices to perform vaginal "rejuvenation," cosmetic vaginal procedures, or non-surgical vaginal procedures to treat symptoms related to menopause, urinary incontinence, or sexual function may be associated with serious adverse events. The safety and effectiveness of energy-based devices for treatment of these conditions has not been established.

GSM

OSPEDALE SAN RAFFAELE

FDA Warns Against Use of Energy-Based Devices to Perform Vaginal 'Rejuvenation' or Vaginal Cosmetic Procedures: FDA Safety Communication

Date Issued:

July 30, 2018

Summary of Problem and Scope:

We are aware that certain device manufacturers may be marketing their energy-based medical device for vaginal "rejuvenation" and/or cosmetic vaginal procedures. The safety and effectiveness of energy-based medical devices to perform these procedures has not been established.

Vaginal "rejuvenation" is an ill-defined term; however, it is sometimes used to describe non-surgical procedures intended to treat vaginal symptoms and/or conditions including, but not limited to:

- Vaginal laxity
- Vaginal atrophy, dryness, or itching
- Pain during sexual intercourse
- Pain during urination
- Decreased sexual sensation

To date, we have not cleared or approved for marketing any energy-based devices to treat these symptoms or conditions, or any symptoms related to menopause, urinary incontinence, or sexual function. The treatment of these symptoms or conditions by applying energy-based therapies to the vagina may lead to serious adverse events, including vaginal burns, scarring, pain during sexual intercourse, and recurring/chronic pain.

GSM

FDA Warns Against Use of Energy-Based Devices to Perform Vaginal 'Rejuvenation' or Vaginal Cosmetic Procedures: FDA Safety Communication

Date Issued:
July 30, 2018

Recommendations for Patients:

- Be aware that the safety and effectiveness of energy-based devices to perform vaginal "rejuvenation" or cosmetic vaginal procedures has not been established.
- Understand that the FDA has not cleared or approved any energy-based medical device for vaginal "rejuvenation" or vaginal cosmetic procedures, or for the treatment of vaginal symptoms related to menopause, urinary incontinence, or sexual function.
- Discuss the benefits and risks of all available treatment options for vaginal symptoms with your health care provider.
- If you have undergone treatment for vaginal "rejuvenation" and experienced a complication, you are encouraged to file a report through MedWatch, the FDA Safety Information and Adverse Event Reporting program (/Safety/MedWatch/HowToReport/ucm085568.htm).

GSM

FDA Warns Against Use of Energy-Based Devices to Perform Vaginal 'Rejuvenation' or Vaginal Cosmetic Procedures: FDA Safety Communication

Date Issued:
July 30, 2018

Recommendations for Health Care Providers:

- Be aware that the safety and effectiveness of energy-based devices to perform vaginal "rejuvenation" or cosmetic vaginal procedures has not been established.
- Understand that the FDA has not cleared or approved any energy-based medical device for vaginal "rejuvenation" or vaginal cosmetic procedures, or for the treatment of vaginal symptoms related to menopause, urinary incontinence, or sexual function.
- Discuss the benefits and risks of all available treatment options for vaginal symptoms with your patients.
- If any patients experience adverse effects from procedures that involved the use of energy-based devices to perform vaginal "rejuvenation", cosmetic procedures, or treat genitourinary symptoms of menopause, sexual dysfunction, or urinary incontinence, please file a report through MedWatch, the FDA Safety Information and Adverse Event Reporting program (/Safety/MedWatch/HowToReport/ucm085566.htm).

GSM

FDA Warns Against Use of Energy-Based Devices to Perform Vaginal 'Rejuvenation' or Vaginal Cosmetic Procedures: FDA Safety Communication

FDA Activities:

We are aware that certain device manufacturers may be inappropriately marketing their energy-based devices for the uses noted above that are outside of their cleared or approved intended uses. We have contacted (/MedicalDevices/ResourcesforYou/Industry/ucm111104.htm) these manufacturers to share our concerns and will be monitoring their claims about uses of their products.

In addition, we will continue to monitor reports of adverse events associated with this issue and will keep the public informed if significant new information becomes available.

Reporting Problems to the FDA:

Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with procedures marketed as vaginal "rejuvenation". If you experience adverse events associated these procedures, we encourage you to file a voluntary report through MedWatch (/Safety/MedWatch/default.htm), the FDA Safety Information and Adverse Event Reporting program. Health care personnel employed by facilities that are subject to FDA's user facility reporting requirements (/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/default.htm) should follow the reporting procedures established by their facilities.

GSM

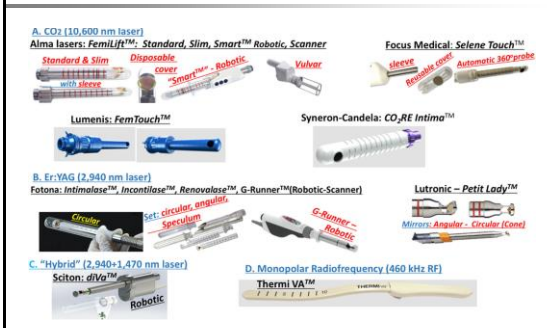


Fig. 7. Energy-based probes for vaginal and vulvar treatment listed in alphabetic order. (Courtesy: manufacturers).

GSM

ENERGY BASED DEVICES

- Radiofrequency
  - – 7 studies in peer reviewed journals
- LASER
  - – 64 studies in peer reviewed journals

DISCLOSURES

Lasers in Surgery and Medicine 49:137–159 (2017)

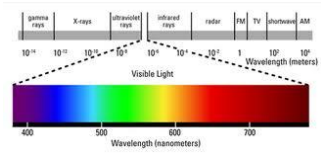
Light and Energy Based Therapeutics for Genitourinary Syndrome of Menopause: Consensus and Controversies

Yona Tadir, MD,[1]* Adrian Gaspar, MD,[2] Abinoam Lev-Sagie, MD,[3] Macrene Alexiades, MD, PhD,[4] Red Alinsod, MD,[5] Alex Bader, MD,[6] Alberto Calligaro, MD,[7] Jorge A. Elias, MD,[8] Marco Gambaciani, MD,[9] Jorge E. Gaviria, MD,[10] Cheryl B. Iglesia, MD,[11] Ksenija Selih-Martinec, MD,[12] Patricia L. Mwesigwa, MD,[11] Ureka B. Ogrinc, MSc, MD,[13] Stefano Salvatore, MD,[14] Paolo Scollo, MD,[15] Nicola Zerbinati, MD,[16] and John Stuart Nelson, MD, PhD[17]

TABLE 3. Vaginal Rejuvenation for Enhancement of Sexual Gratification

Author	Indication	*N*	Device	Findings	Complic.
Millheiser et al. (2010) [96]	Laxity after childbirth	24 at 3 months	Monopolar RF	All subjects with improved vaginal tightness at 1 month; sustained or further improved by 3 months	None
Lee (2014) [97]	Laxity	30 at 2 months	Er:YAG	Perineometer values improved in all patients, 70% subjective improvement	None
Vicariotto and Raichi (2016) [98]	Laxity	11 at 2 months (premenopausal, vaginal laxity arm). 12 at 2 months (postmenopausal, VVA/GSM arm)	Dynamic quadripolar radiofrequency (DQRF)	Improvement reported at 4–8 weeks in laxity and urinary symptoms, VVA symptoms, and sexual satisfaction	None

LASER



Wavelengths of medical lasers
UV – Visible– 10600nm (IR)

Wavelength: expressed in nanometer (nm)

GSM

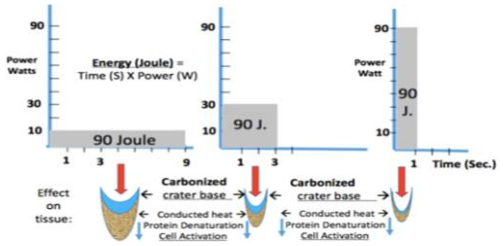


Fig. 4. Energy (Joule) = Power (Watt) × Time (Second). Effect on tissue is different even if the same energy is deposited depending on exposure time. Same energy may cause different effect, that is, crater shape, superficial carbonization, and thermal coagulation. Three examples of same energy, 90 J, will cause different effect on the tissue. (Courtesy: Tadir Y).

DISCLOSURES

Lasers in Surgery and Medicine 49:137–159 (2017)

Light and Energy Based Therapeutics for Genitourinary Syndrome of Menopause: Consensus and Controversies

Yona Tadir, MD,[1]* Adrian Gaspar, MD,[2] Abinoam Lev-Sagie, MD,[3] Macrene Alexiades, MD, PhD,[4] Red Alinsod, MD,[5] Alex Bader, MD,[6] Alberto Calligaro, MD,[7] Jorge A. Elias, MD,[8] Marco Gambaciani, MD,[9] Jorge E. Gaviria, MD,[10] Cheryl B. Iglesia, MD,[11] Ksenija Selih-Martinec, MD,[12] Patricia L. Mwesigwa, MD,[13] Urska B. Ogrinc, MSc. MD,[13] Stefano Salvatore, MD,[14] Paolo Scollo, MD,[15] Nicola Zerbinati, MD,[16] and John Stuart Nelson, MD, PhD[1]

TABLE 1. Technical Parameters of Vaginal Probes Listed in Manufacturer's Alphabetic Order (Courtesy: Manufacturers)

Brand name	Laser type/ wavelength (nm) or RF	Pulse duration (ms)	Maximum energy/pulse (mJ)	Surface area "lased"/ exposure (mm^2)
Alma Lasers, Buffalo Grove, IL. Fotona, San Clemente, CA.	CO_2 – 10,600 Er:YAG – 2,940	400 250	500 (per pixel) 240 J (per pass) 3 J/cm^2	10 80 (cm^2), non-ablative, entire surface
Focus Medical, Bethel, CT. Lumenis, San Jose, CA. Lutronic Aesthetics, Burlington, MA.	CO_2 – 10,600 CO_2 – 10,600 Er:YAG – 2,940	1–200 NA 0.2 ~ max. 1500 (Dual mode)	60 7.5/10/12.5 3.7 J (per pulse)	10 NA 144 (per pulse)
Sciton, Inc. Palo Alto, CA. Syneron-Candela, Irvine, CA. ThermiVA, Irving, TX.	Hybrid: 2,940/1,470 CO_2 – 10,600 RF 460 kHz	150/20 20–1,066 –	300/100 70 Estimated tissue temp. 47°C	1.5–2.5 10 10

NA: not available.

MICROABLATIVE FRACTIONAL CO2 LASER

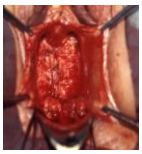
Histological study on the effects of microablative fractional CO2 laser on atrophic vaginal tissue: an ex vivo study.

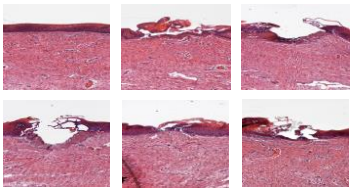
Salvatore S, Leone Roberti Maggiore U, Athanasiou S, Origoni M, Candiani M, Calligaro A, Zerbinati N.

Menopause. 2015 Jan 20. [Epub ahead of print]

PMID: 25608269

An ex-vivo study on vaginal specimens collected during recontructive pelvic surgery demonstrated connective tissue remodeling after treatment with a fractional CO_2 laser without damage or side-effects and predetermined parameters





DISCLOSURES

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K133895

Device Name
DEKA Smartxide2

Indications for Use *(Describe)*

It is indicated for incision, excision, ablation, vaporization and coagulation of body soft tissues in medical specialties including aesthetic (dermatology and plastic surgery), podiatry, otolaryngology (ENT), gynaecology, neurosurgery, orthopaedics, general and thorasic surgery (including open and endoscopic), dental and oral surgery and genitourinary surgery. The use with the scanning unit is indicated for ablative skin resurfacing.

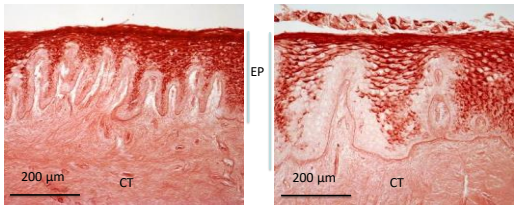
ADVERSE EVENTS AS RECORDERED BY FDA ON SMARTXIDE2 AND SMARTXIDE TOUCH from January 1st, 2015 to July 31st, 2018.

Seven adverse events reported

- 2 physician injuries (error in connecting the scanner to the articulated arm)
- 1 performed in MRKH syndrome
- 2 in CPP/IC subjects
- 2 complications of burning feeling in the urethra/vagina treated with medications (no further action)

~ 1000 equipments in US

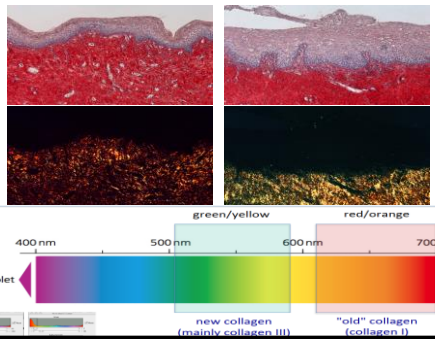
MICROABLATIVE FRACTIONAL CO2 LASER



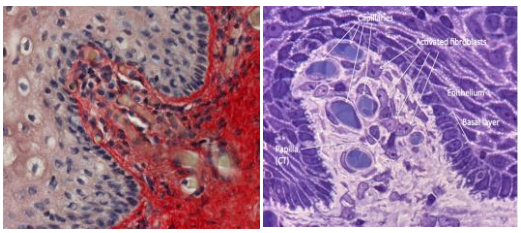
Postmenopausal vaginal mucosa

Postmenopausal vaginal mucosa
1 month after fractional CO_2 laser treatment

MICROABLATIVE FRACTIONAL CO2 LASER

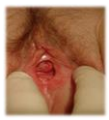


MICROABLATIVE FRACTIONAL CO2 LASER



WHAT IS THE EVIDENCE?

Efficacy?



- Vulvovaginal Atro… (VA)

- Sex…

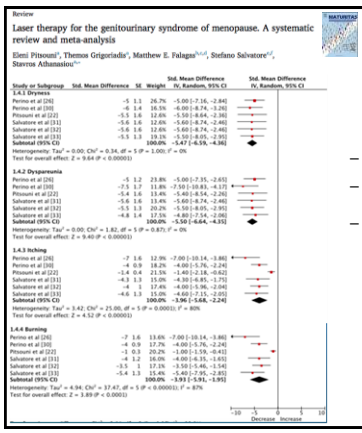
GSM

- Lower …y Tract Symptoms (LUTS)

Review

Laser therapy for the genitourinary syndrome of menopause. A systematic review and meta-analysis

Eleni Pitsouni[a], Themos Grigoriadis[b], Matthew E. Falagas[b,c,d], Stefano Salvatore[e,f], Stavros Athanasiou[b,*]



Maturitas 103 (2017) 78–88

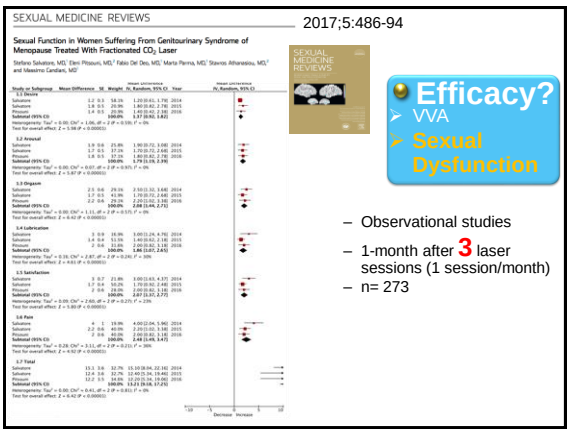
Efficacy?
- VVA

- Observational studies
- 1-month after **3** laser sessions (1 session/month)
- n= 255

SEXUAL MEDICINE REVIEWS 2017;5:486-94

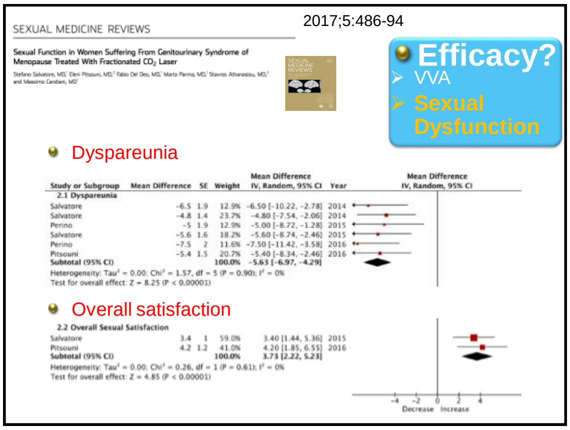
Sexual Function in Women Suffering From Genitourinary Syndrome of Menopause Treated With Fractionated CO_2 Laser

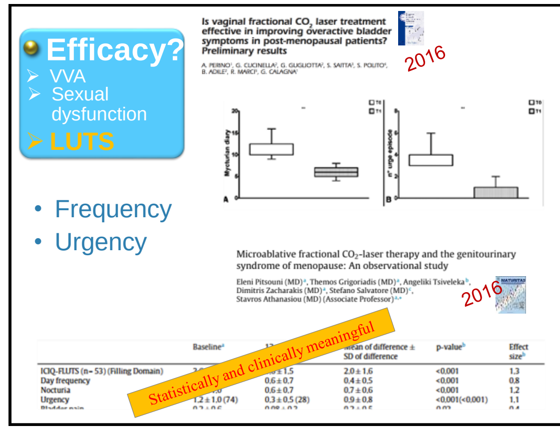
Stefano Salvatore, MD,[1] Eleni Pitsouni, MD,[2] Fabio De Ceo, MD,[1] Marta Parma, MD,[1] Stavros Athanasiou, MD,[2] and Massimo Candiani, MD[1]

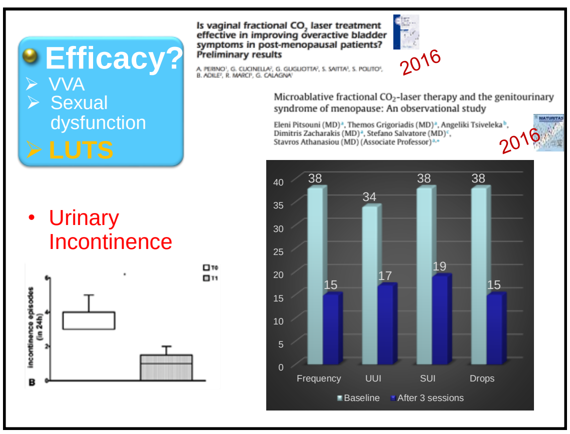


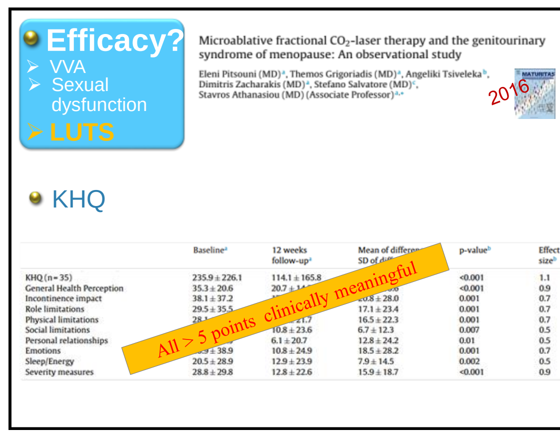
Efficacy?
- VVA
- **Sexual Dysfunction**

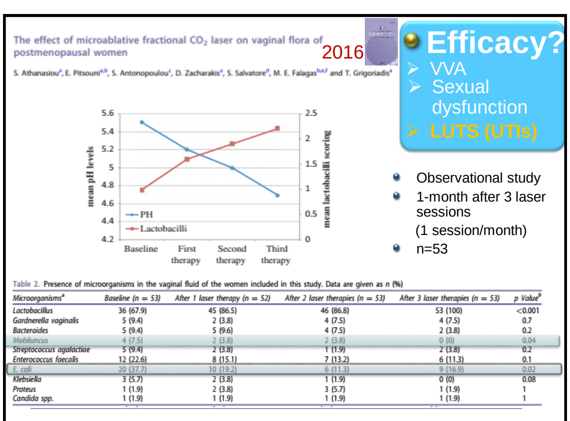
- Observational studies
- 1-month after **3** laser sessions (1 session/month)
- n= 273

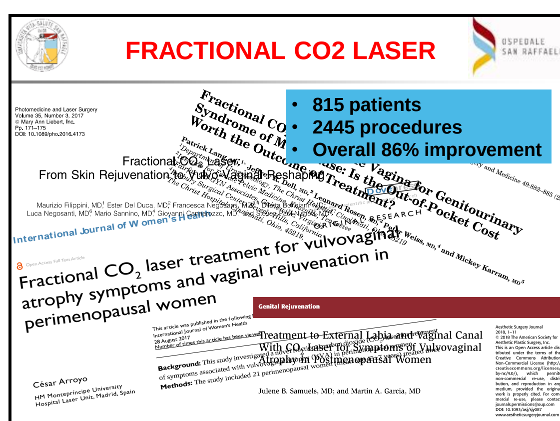

SEXUAL MEDICINE REVIEWS
2017;5:486-94
Sexual Function in Women Suffering From Genitourinary Syndrome of Menopause Treated With Fractionated CO2 Laser
Efficacy?
VVA
Sexual Dysfunction
Dyspareunia
2.1 Dyspareunia
Overall satisfaction
2.2 Overall Sexual Satisfaction
Decrease Increase


Is vaginal fractional CO2 laser treatment effective in improving overactive bladder symptoms in post-menopausal patients? Preliminary results
2016
Efficacy?
VVA
Sexual dysfunction
LUTS
Frequency
Urgency
Microablative fractional CO2-laser therapy and the genitourinary syndrome of menopause: An observational study
2016
Statistically and clinically meaningful


Is vaginal fractional CO2 laser treatment effective in improving overactive bladder symptoms in post-menopausal patients? Preliminary results
2016
Efficacy?
VVA
Sexual dysfunction
LUTS
Microablative fractional CO2-laser therapy and the genitourinary syndrome of menopause: An observational study
2016
Urinary Incontinence
Frequency
UUI
SUI
Drops
Baseline
After 3 sessions


Efficacy?
VVA
Sexual dysfunction
LUTS
Microablative fractional CO2-laser therapy and the genitourinary syndrome of menopause: An observational study
2016
KHQ
All > 5 points clinically meaningful


The effect of microablative fractional CO2 laser on vaginal flora of postmenopausal women
2016
Efficacy?
VVA
Sexual dysfunction
LUTS (UTIs)
Observational study
1-month after 3 laser sessions
(1 session/month)
n=53


FRACTIONAL CO2 LASER
815 patients
2445 procedures
Overall 86% improvement
Fractional CO2 laser treatment for vulvovaginal atrophy symptoms and vaginal rejuvenation in perimenopausal women
Treatment to External Labia and Vaginal Canal With CO2 Laser for Symptoms of Vulvovaginal Atrophy in Postmenopausal Women

EUGA® EUROPEAN UROGYNAECOLOGICAL ASSOCIATION

10th Annual Congress Leading Lights in Urogynaecology

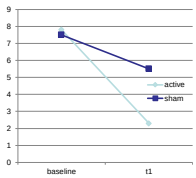
A double-blind randomised controlled trial of microablative fractional CO_2 laser vs sham therapy on patients with vaginal dryness linked sexual function limitations: an interim analysis

S. Girardelli, E. Pitsouni, E. Marotta, M. Parma, M. Candiani, S. Athanasiou, S. Salvatore

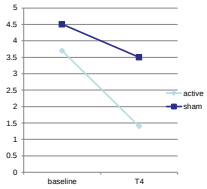
RESULTS

OSPEDALE SAN RAFFAELE

Vaginal Dryness



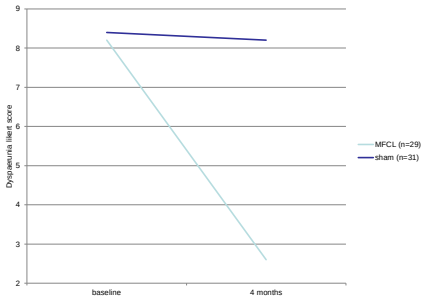
Burning



Vaginal Dryness	Baseline	T4	p - value
Active	7.8	2.3	< 0.05
Sham	7.5	5.5	> 0.05

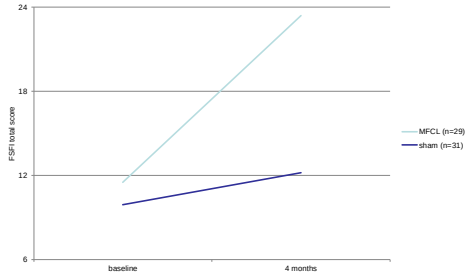
Changes in dyspareunia

OSPEDALE SAN RAFFAELE



Changes in FSFI

OSPEDALE SAN RAFFAELE



GSM - CONCLUSION

OSPEDALE SAN RAFFAELE

- Different effective treatment available
- Need to improve evidence for many (?all) of them
- Confusion in evaluating energy based devices available on the market and need to discriminate amongst them

Thank you for your attention!

Obstetrics and Gynaecology Unit – Vita-Salute San Raffaele University and San Raffaele Hospital – Milan, Italy

ADVERSE EVENTS AS RECORDERED BY FDA ON SMARTXIDE2 AND SMARTXIDE TOUCH from January 1st, 2015 to July 31st, 2018.

Model Number M110C1
Device Problems Human Factors Issue; Adverse Event Without Identified Device or Use Problem
Event Date 03/09/2018
Event Type Injury **Date March 9th 2018**
Manufacturer Narrative https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=7424573&pc=GEX

The actual device was not returned to the manufacturer for evaluation. Us importer's authorized service personnel checked the actual device unit at customer site on march 15th, 2018. The technician found, prior to any servicing operation, the device to be working properly within specifications. The technician found that the scanner assembly was well secured to the articulated arm at the time of his inspection. Then, he removed the scanner assembly from the articulated arm in order to fully inspect the device. After all the inspection he has not performed any intervention because the device was working properly. He spoke with the physician that admitted that he did not even know that the scanner could be detached/unscrewed. The technician remarked to the physician to frequently check the right coupling of the scanner to the articulated arm ((b)(4)). The investigation carried out did not conclude that a design deficiency or device malfunctioning was responsible for causing the event. Rather, it could be assumed that there was a human factors issue, where a failure of the operator to appropriately secure the scanner to the articulated arm before starting the use of the device, contributed to event. By manufacturer's investigation the operator's manual and risk analysis are adequate. Device working within specifications. No remedial action required. This initial report is to be considered as final report, unless fda has further questions.

Event Description

(b)(4) (us importer) (b)(4) reports of an adverse event happened at (b)(6), us involving a smartxide touch laser medical device (ref: m110c1 - s/n: (b)(4)) manufactured by el. En. Electronic engineering (b)(4). Based on the investigation performed by (b)(4) personnel they found that the scanner has detached from the device's articulated arm during a treatment and fired upon the physician's neck. (b)(4) reports that,despite numerous attempt to contact the customer, it was unresponsive and no additional information related to the injury occured to the physician, parameter used and procedure was received. This incident was classified as a reportable event by the us importer due to the injury reported by the operator (according to fda 21 cfr part 803 - assumed as a worst case scenario, on the side of caution) and because the detachment of the scanner caused an accidental radiation occurence (according to fda 21 cfr part 1000-1040). This aro is reported to the fda under the mdr procedure according to fda 21 cfr part 1003. 10. 1. C). The us importer, (b)(4) located in (b)(4), submitted an mdr initial report to fda for this event (#1222993-2018-00006) on march 27th, 2018. (b)(4). Also represents us distributor and service center for el. En. Electronic engineering (b)(4). Medical devices. We, the manufacturer of device, became aware of the event on march the 26th, 2018 by email from the us importer and, according to 21 cfr part 803. 50(b)(2), submitted to fda an own mdr report in order to conduct an investigation of the event and to obtain missing or incomplete information provided by the importer.

ADVERSE EVENTS AS RECORDERED BY FDA ON SMARTXIDE2 AND SMARTXIDE TOUCH from January 1st, 2015 to July 31st, 2018.

Model Number M103P1
Device Problem Adverse Event Without Identified Device or Use Problem
Event Date 08/23/2017
Event Type Injury https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=7125417&pc=GEX
Event Description

The patient contacted the manufacturer through the general contact mail in date (b)(6) 2017 reporting of an adverse event following a treatment with smartxide2 laser medical device (ref: m103p1 - s/n: (b)(4)) manufactured by el. En. Electronic engineering (b)(4). The patient described that she saw an urologist because she was having burning in her urethra following 4 laser treatment performed by doctor (b)(6) at the clinic "advanced urology manhasset" placed at (b)(6). That patient saw 2 different urologist and received medical intervention from them after the laser treatments. The manufacturer have involved its us importer, (b)(4) company located in (b)(4), in order to carry the investigation in the united states. The us importer has been informed the same day that the manufacturer became aware of the event ((b)(6) 2017). (b)(4). Also represents us distributor and service center for el. En. Electronic engineering (b)(4) medical devices. The us importer have contacted both patient and physician in order to deeply investigate on this issue. Unfortunately the patient did not agreed to release her clinical data for evaluation. This incident was classified as a reportable event by the us importer because the patient had medical intervention following the treatment. The us importer, (b)(4), submitted an mdr initial report to fda for this event (#1222993-2017-00050) on december, 15, 2017. This medwatch report is in response to fda report mw5073422 submitted to fda by the patient in date (b)(6) 2017 and received by fda in date (b)(6) 2017. In conformity to 21 cfr part 803. 22(a) el. En. Will submit only one mdr because the information incoming from different sources (the patient and fda) concerns the same event. We, the manufacturer of device, became aware of the event on (b)(6) 2017 by email from the patient and, according to 21 cfr part 803. 50(b)(2), submitted to fda an own mdr report in order to conduct an investigation of the event and to obtain missing or incomplete information provided by the importer.

Manufacturer Narrative

The actual device was not returned to the manufacturer for evaluation. Us importer's authorized service personnel checked the actual device unit at customer site on december 11th, 2017. The technician found, prior to any servicing operation, the device to be working properly within specifications ((b)(4)). The investigation has been performed by interrogating the doctor that have performed the treatment, dr. (b)(6). The operator of the device (site doctor) stated that the treatment procedure was performed per the clinical reference guide protocol. Moreover site's doctor did indicate the patient has a history of cystitis, long standing urethral pain prior to the laser procedures, was on numerous medications for +25 years (such as elmiron, amytriptyline, loprezol, atosvastatin, gabapentin, valium, oxycodone, pro-biotics, calcium, vitamin d) , and was looking for urethra pain management treatments. However the patient declined to follow up with the customer site, so there is no additional information regarding the treatment from this event. The investigation carried out did not conclude that a design deficiency or device malfunctioning was responsible for causing the event. Rather, it could be assumed that there was a pre-existing patient's condition that contributed to the event. Device working within specifications. No remedial action required. This initial report is to be considered as final report, unless fda has further questions.

ADVERSE EVENTS AS RECORDERED BY FDA ON SMARTXIDE2 AND SMARTXIDE TOUCH from January 1st, 2015 to July 31st, 2018.

Model Number M110C1
Device Problems Use of Device Problem; Adverse Event Without Identified Device or Use Problem
Event Date 09/04/2017
Event Type Injury https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=6840977&pc=GEX
Manufacturer Narrative

The actual device was not returned to the manufacturer for evaluation. Us importer's authorized service personnel checked the actual device unit at customer site on july 28th, 2017. The technician found, prior to any servicing operation, the device to be working properly within specifications. The technician found that the scanner assembly was well secured to the articulated arm at the time of his inspection. Then, he removed the scanner assembly from the articulated arm in order to fully inspect the device. The threads of both scanner and articulated arm was found in a good state without any visible signs of damage or wear. Technician also evaluate that no unexpected laser beam was present at the end of the articulated arm. After all the inspection he has not performed any intervention because the device was working properly. He then proceeded to firmly secure the scanner to the articulated arm and advised the physician to check frequently the connection between articulated arm and scanner in order to ensure that is well secured ((b)(4)). The investigation carried out did not conclude that a design deficiency or device malfunctioning was responsible for causing the event. Rather, it could be assumed that there was a human factors issue, where a failure of the operator to appropriately secure the scanner to the articulated arm during cleaning/ set-up of the device, contributed to event. By manufacturer's investigation the operator's manual and risk analysis are adequate. Device working within specifications. No remedial action required. This initial report is to be considered as final report, unless fda has further questions.

Event Description

(b)(4) (us importer) mr. (b)(6) reports of an adverse event happened at (b)(6) involving a smartxide touch laser medical device (ref: m110c1 - s/n: (b)(4)) manufactured by el. En. Electronic engineering (b)(4). Based on the investigation performed by (b)(4) personnel they found that the scanner has detached from the device's articulated arm during a treatment and fired upon the physician's hand. (b)(4) reports that, despite numerous attempt to contact the customer, it was unresponsive and no additional information related to the injury occured to the physician, parameter used and procedure was received. Also the date of the event is unknown. This incident was classified as a reportable event by the us importer due to the injury reported by the operator (according to fda 21 cfr part 803 - assumed as a worst case scenario, on the side of caution) and because the detachment of the scanner caused an accidental radiation occurence (according to fda 21 cfr part 1000-1040). This aro is reported to the fda under the mdr procedure according to fda 21 cfr part 1003. 10. 1. C). The us importer, (b)(4) located in (b)(4), submitted an mdr initial report to fda for this event (#1222993-2017-00036) on august 10th, 2017. (b)(4) also represents us distributor and service center for el. En. Electronic engineering (b)(4) medical devices. We, the manufacturer of device, became aware of the event on august the 8th, 2017 by email from the us importer and, according to 21 cfr part 803. 50(b)(2), submitted to fda an own mdr report in order to conduct an investigation of the event and to obtain missing or incomplete information provided by the importer.

ADVERSE EVENTS AS RECORDERED BY FDA ON SMARTXIDE2 AND SMARTXIDE TOUCH from January 1st, 2015 to July 31st, 2018.

Model Number M110B1
Device Problems Use of Device Problem; Improper or Incorrect Procedure or Method
Event Date 04/13/2017
Event Type Injury https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=6489470&pc=GEX
Event Description

El. En. 's service department became aware of an adverse event in which is involved the laser medical device smartxide touch model number m110b1, s/n (b)(4), manufactured by el. En. Electronic engineering (b)(4). The event have been reported to el. En. 's service personnel from clinical engineering department of (b)(6) (health care facility) that states that a female patient (age and name are unknown) have reported an intense reaction to the treatment during a gynaecological treatment with the above mentioned laser medical device and accessory 360° vaginal probe (code m93501) in which, at the very beginning of the treatment, the physician noticed smoke coming out from the handpiece. The physician immediately stopped the treatment and turned the device off. El. En. 's product specialist contacted the physician, that have used the actual device involved in the event, in order to obtain additional information about the state of health of the patient. The physician reported that the patient did not have any injury or adverse reaction following the event. The actual laser medical device and accessory involved in this adverse event are not marketed in the us territory. No unit of this particular device and accessory has ever been delivered to the us. A similar device model number m110c1 and a similar accessory 90° side-firing handpiece with cylindrical body (code m94601) is marketed in the us with premarket clearance 510(k) n° k133895 and following letter to file. The actual date of the event is unknown. Event took place in the (b)(6). We, the manufacturer of device, became aware of the event on march the 30th, 2017 by email from (b)(6) clinical engineering department and, according to 21 cfr part 803, submitted to fda an mdr report because, even if there is no injury to patient, this is an event that if it will have to recur could possibly lead to a serious injury to patient (potential adverse event).

Manufacturer Narrative

The actual device was not returned to the manufacturer for evaluation. El. En. 's service personnel checked the actual suspected device unit at customer site on april 3rd, 2017. El. En. Service technician evaluated the device for calibration and performance of laser and accessories. The smartxide touch unit and relevant accessories were determined to be operating properly within their specifications. No failure detected (el. En. 's service report (b)(4)). El. En. 's service personnel interviewed both the physician and clinical engineering specialist, and they confirmed that the patient was submitted to a gynaecological treatment and, at the beginning of it, the physician saw smoke coming out from the handpiece and immediately stopped the treatment and turned the device off. The physician reported that the patient was not injured and did not require any medical intervention afterwards. (b)(6) clinical engineering and physician reported that a piece of paper cleaning towel was found inside the cavity to the handpiece. The piece of paper towel was left, unintentionally, inside the handpiece by the nurse in charge of the reprocessing of it, during the thorough cleaning that has to be performed before sterilization. The handpiece was sterilized with the paper cleaning towel inside. The residual paper towel immediately ignited when the laser has been activated and the beam passed through the handpiece body. Operator's manual (code om110b1_ij, provided by el. En. Together with the device, specifically requires (chapter 14. 1. 2 - "co2 reusable parts reprocessing") to check the presence of any kind of débrides residual on the handpiece and proceed to totally remove them before proceeding with the sterilization process. Reusable accessories reprocessing procedure were not followed as per operator's manual. The user did not apply the appropriate attention during the required inspection of the accessory in order to detect the presence of any foreign material present in it before proceeding to the sterilization of the accessory itself. The investigation carried out did not conclude that a design deficiency or device malfunctioning was responsible for causing the event. Rather, it could be assumed that there was a human factors issue, where a failure to appropriately reprocess the accessories, contributed to event. By manufacturer's investigation the operator's manual and risk analysis are adequate. Device working within specs. No remedial actions required. This initial report is to be considered as final report, unless fda has further questions.

ADVERSE EVENTS AS RECORDERED BY FDA ON SMARTXIDE2 AND SMARTXIDE TOUCH from January 1st, 2015 to July 31st, 2018.

Model Number M103P1
Device Problem Insufficient Information
Event Date 03/31/2016
Event Type Injury https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=5989901&pc=GEX
Manufacturer Narrative

The event has been reported by the fda to the us importer, (b)(4), via mail, following an adverse event reported by one patient through the medwatch program (report code mw5062264). The communication to the us importer has been forwarded by the fda on july 25th, 2016. The us importer forwarded the information to el. En. Electronic engineering (b)(4), manufacturer of the smartxide2 laser, on september 26th, 2016, via email. El. En. (b)(4) decided to submit this initial mdr to the fda, as soon as it received the information from the us importer (b)(4) and also started an investigation into this event, with the support of (b)(6), which is the official us importer and distributor of this medical device in the usa. At this time, this is the only information el. En. Electronic engineering (b)(4) has, regarding this event. The investigation has just started and has not given any further results, yet. El. En. Electronic engineering (b)(4) will of course submit a follow-up report to the fda, with any additional information that could be found, during such investigation. Device not available at the time.

Manufacturer Narrative

Since the actual device was not returned to the manufacturer, a direct investigation on the device could not be performed. Based on the information provided in the medwatch program report code mw5062264, el. En. (b)(4), as manufacturer of the suspect laser medical device involved in the adverse event happened to ms. (b)(6), have attempted to contact the patient by phone and by email (the only contact details expressed in the mw5062264 report). Also the us importer, (b)(4) , was involved in the attempt to contact ms. (b)(6) in order obtain any additional information for the investigation. All the attempts to contact ms. (b)(6), done by both el. En. And (b)(4), have failed. Infact the email address provided in the report mw5062264 could not be reached by e-mail providers and she did not ever answered the phone and no voicemail was present in order to leave a message. Throughout october 2016, (b)(4) and el. En. Have done 4° 3 attempts to contact ms. (b)(6) by email and 4° 3 attempts to contact her by phone without any success nor reply. Based on the information above mentioned is impossible to investigate on this case any further. El. En. Will remain vigilant with increased level of attention on this matter. Therefore, this specific case is to be classified as closed, unless fda has further questions.

Event Description

On september 26th, 2016, el. En. Electronic engineering (b)(4) became aware of an adverse event, reported by one patient to the fda, through the medwatch system. The patient, mrs (b)(6), reported to the fda, on may 12th, 2016, an adverse event happened to her, following what she describes as a "vaginal rejuvenation treatment", performed by her gynecologist with the "monalisa touch laser", on (b)(6) 2016. With high degree of confidence, the medical device involved in this event is the deka smartxide2 laser, because this is the only medical device marketed in the usa, to perform the "monalisa touch" procedure, at the time the patient received the treatment. El. En. Electronic engineering (b)(4) is the manufacturer of the deka smartxide2 laser medical device, cleared by fda under 510(k) k133895. The patient reported that, the day after the treatment, she developed a severe and debilitating bladder/urethral pain. In the following 2 weeks, she was twice visited by the gynecologist, who had performed the treatment, having also urinalysis, always with negative responses. Then the patient changed gynecologist and this new gynecologist was treating her, at the time she submitted the report, with vagifem, which is however medication to treat gsm symptoms and definitely not the primary care for the symptoms that the patient reported. So, there may be additional clinical information, which we may lack, in this particular event. The bladder/urethral pain reported by the patient might be compatible with a form of uti, even if, with the information in our hand, it is impossible to prove it. As per the operator's manual (p/n om103p1. g. V08) of the laser and the monalisa touch clinical reference guidelines (p/n 921-7030-000, rev. 03), both pain and infections may be foreseeable side effects of the treatment. Fda communicated this event to (b)(4), us importer of the medical device, on july 25th, 2016, but the letter was only received few days ago. Then, el. En. Electronic engineering (b)(4), the manufacturer, has been informed via email, by (b)(4) (us importer), on septembre 26th, 2016, only. We suspect that the patient saw the brand name of the laser (deka) and put it in the "manufacturer" field of the report, where it is, in fact, only specified "deka". Then, the fda sent the communication to the us importer, (b)(4) and not to el. En. Electronic engineering (b)(4). Also, the main distributor of this medical device in the usa is (b)(4), which is the official us importer for this device, too.

ADVERSE EVENTS AS RECORDERED BY FDA ON SMARTXIDE2 AND SMARTXIDE TOUCH from January 1st, 2015 to July 31st, 2018.

Model Number M103P1
Device Problem Adverse Event Without Identified Device or Use Problem
Event Date 02/11/2016
Event Type Injury https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=5846168&pc=GEX
Event Description

North america importer/distributor, (b)(6) located in (b)(6) usa, noticed us about an adverse event they recently became aware of. Involved device was deka smartxide2 model number m103p1, s/n (b)(4), manufactured by el. En. Electronic engineering (b)(4). The actual date of event is (b)(6) 2016 and (b)(6) became aware of this incident on august 7th, 2016. Event took place in the united states territory at (b)(6), usa. (b)(6) investigator collected information from customer and informed us that one deka smartxide2 was involved in laser treatment on patient who developed irritation and pain. Moreover he informed us that after the treatment with the deka smartxide2 device the patient received medical intervention from an urgent care clinic. Patient was prescribed clobetasol cream, cymbalta, and diflucan as intervention medication for post treatment care. (b)(6) have submitted an mdr report, concerning this event, for the laser medical device involved, on august 3rd,2016: report (b)(4) for the deka smartxide2 device as importer. The manufacturer of this device is el. En. Electronic engineering (b)(4) we, the manufacturer of device deka smartxide2 , became aware of the event on july 18th, 2016 by email from (b)(6) and, according to 21 cfr part 803, el. En. Electronic engineering (b)(4) submitted to fda an own initial 30 days mdr report for the deka smartxide2 device for which el. En electronic engineering (b)(4) is the manufacturer. This event is reportable to fda, on the side of caution, because the patient received medical intervention to avoid a permanent impairment of a body structure.

Manufacturer Narrative

The actual device was not returned to the manufacturer's for evaluation. U. S local authorized service engineer ((b)(6)) checked the actual suspected device unit at customer site on behalf of manufacturer on july 15th, 2016. (b)(6) service technician evaluated the device for calibration and performance of laser and accessories. The deka smartxide2 unit and relevant accessories were determined to be operating properly within their specifications. No failure detected ((b)(6)). Treatment parameters, used by the physician at the time of the event, were not made available by the physician. The investigation carried out did not conclude that a design deficiency or device malfunctioning was responsible for causing the event. Rather, the injuries reported by the patient are classified as forseeable side effects of the laser treatment. In fact, the operator manual code om103p1. g. V04 (current release delivered with the medical device) in section 10. 1. 2 ' side effects' reports that moderate pain, blood spill, swelling (blood spill and swelling can be reconducted to serious irritation of the skin) are complication that can occur. This event is, anyway, reportable because the patient sought medical intervention from an urgent care clinic. Patient was prescribed clobetasol cream, cymbalta, and diflucan as intervention medication for post treatment care. No failure detected in the actual device evaluated. Device working within specs. Based on that, no remedial actions are required. This initial report is to be considered as final report, unless fda has further questions. Evaluation performed by local service.

ADVERSE EVENTS AS RECORDERED BY FDA ON SMARTXIDE2 AND SMARTXIDE TOUCH from January 1st, 2015 to July 31st, 2018.

Model Number M103P1
Event Date 08/24/2015
Event Type Injury
Manufacturer Narrative
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=5309544&pc=GEX

The actual device was not returned to the manufacturer for evaluation. Us local authorised service (b)(4) inc. Personnel) checked the actual suspected device unit at customer site on behalf of manufacturer on august 26th 2015. Cynosure service technician evaluated the device for calibration and alignment of laser beam. The deka smartxide2 unit was determined to be operating properly within its specifications. No failure detected (service report # (b)(4)). Treatment parameters used by physician were within clinical guidelines. The patient was treated with hiscan dot handpiece for gynaecological treatments which requires the introduction of the probe inside the vaginal canal. This kind of procedure is not suitable for patient having history of rare congenital mullerian agensis (mayer-rokitansky-kuster-hauser syndrome). The laser treatment performed by the physician was incompatible with pre-existing patient conditions. Incompatibility between the laser treatment procedure performed by physician and congenital mayer-rokitansky-kuster-hauser syndrome, suffered by the patient, has been confirmed by person qualified to make a medical judgment. The investigation carried out did not conclude that a design deficiency or device malfunctioning was responsible for causing the event. Rather, it could be assumed that there was a human factors issue, where a failure to appropriately use the device according to pre-existing patient conditions, contributed to event. The physician did not observe the instructions for use provided by the manufacturer together with the laser device. In particular, the operator's manual (code om103p1. g. V04) specifically requires (paragraph 10. 1. 4 - "pretreatment recommendation") that at the time of the initial visit, the physician will determine the suitability of laser treatment and inform the patient about the treatment. The operator manual also requires the physician (paragraph 11. 1 "pre-treatment care - patient examination") to proceed with a visit and anamnesis with evaluation of the patient's medical history. Clinical reference guide (code 921-7030-000), provided by cynosure together with the device, confirms that a screening evaluation is requested to be performed by the physician in order to determine the procedure suitability before treatment. Such evaluation includes medical history and patient questionnaire, physical examination, and an invasive or non-invasive diagnostic examination such as external and internal vaginal examination. A qualified practitioner is solely responsible for evaluating each subject's suitability to undergo laser treatment and for informing those being treated about any risks involved with the treatment, pre and post operative care, and any other relevant information. Redness,irritation, inflammation and discomfort/pain are expected side effects from laser treatments to the anatomic district of the laser procedure as reported by operator manual (paragraph 10. 1. 2 - "side effects"). However in this event, the treatment area was closing, so the patient sought medical intervention in the form of vaginal dilatation procedure. Patient also received estrogen cream/diflucan for preventive post care treatment, generally recommended. Device working within specs. No remedial actions required. El. En. Electronic engineering (b)(4), , manufacturer of the device, never recorded similar adverse event before,compared with more than a (b)(4). This initial report is to be considered as final report, unless fda has further questions.

Event Description

The us importer reported us about an adverse event involving the deka smartxide2 medical laser device, manufactured by el. En. Electronic engineering (b)(4). A patient (female, (b)(6)) received medical intervention (female vaginal dilatation procedure) following a co2 laser treatment by a physician for gynaecological purpose. Patient was feeling pain and developed redness so she sought medical assistance. It was given dilators, estrogen cream / diflucan for post care treatment. Patient has also a history of rare congenital mullerian agensis (mayer-rokitansky-kuster-hauser syndrome). Event occurred at (b)(6) clinic - (b)(6) us. The actual date of event is (b)(6) 2015. The us importer, (b)(4) us, submitted an mdr initial report to fda for this event (# (b)(4)) on november 24th, 2015. (b)(4) inc. Also represents us distributor and service center for el. En. Electronic engineering (b)(4) medical devices. We, the manufacturer of device, became aware of the event on november 25th 2015 by email from the us importer and, according to 21 cfr part 803. 50(2), submitted to fda an own mdr report in order to conduct an investigation of the event and to obtain missing or incomplete information provided by the importer. This event is reportable because the patient received medical intervention.

CO2 LASER
LONG-TERM FOLLOW-UP

- **Observational studies**
- **Up to 36 months**
- **n= 313**

Maintenance of positive results

CO2 LASER
LONG-TERM FOLLOW-UP

Menopause: The Journal of The North American Menopause Society
Vol. 24, No. 7, pp. 810–814
DOI: 10.1097/GME.0000000000000839
© 2017 by The North American Menopause Society

Use of a novel fractional CO_2 laser for the treatment of genitourinary syndrome of menopause: 1-year outcomes

Eric R. Sokol, MD,[1] and Mickey M. Karram, MD[2]

2017

Abstract

Objectives: To assess safety and efficacy of a fractional CO_2 laser therapy for the treatment of genitourinary syndrome of menopause (GSM) with follow-up to 1 year posttreatment.

Methods: Women presenting with GSM and meeting inclusion criterion were enrolled. Visual Analog Scales were used to grade vaginal pain, burning, itching, dryness, dyspareunia, and dysuria. Dilators were used to rate ...

Results: Of 30 women (mean age 58.6 ± 8.8 years), three were lost to follow-up at 3 months and six at 1 year. None were discontinued or withdrew due to an adverse event. Average improvement in Visual Analog Scale scores for all symptom categories was statistically significant at 3 months and remained so through 1 year, except dysuria. Differences between data at 3 months and 1 year were not statistically significant, indicating persistence of positive outcomes. Average overall improvement in pain was 1.9 (±3.4), burning 1.9 (±3.1), itching 1.4 (±1.9), dryness 5.9 (±2.8), dyspareunia 4.9 (±3.3), and dysuria 0.9 (±3.1). Improvement in average Vaginal Health Index and Female Sexual Function Index scores was also statistically significant ($P < 0.0001$). Of 19 women undergoing dilator examination at 1 year, 18 (94.8%) were comfortable with the same or larger dilator size. Twenty-two of 24 women (92%) were satisfied or extremely satisfied with the treatment at 1 year.

women suffering from symptoms of GSM, although additional studies with larger populations and placebo control is needed to confirm these results.

CO2 LASER
LONG-TERM FOLLOW-UP

Safety and long-term efficacy of fractional CO_2 laser treatment in women suffering from genitourinary syndrome of menopause☆

Fariba Behnia-Willison[a], Sara Sarraf[b], Joseph Miller[c,*], Behrang Mohamadi[d], Alison S. Care[e,j], Alan Lam[e], Nadia Willison[f], Leila Behnia[g], Stefano Salvatore[h]

2017

ABSTRACT

Objectives: To evaluate the safety and long-term efficacy of fractional CO_2 laser treatment in reducing the severity of symptoms of genitourinary syndrome of menopause (GSM) in menopausal women.

Study design: 102 women presenting with symptomatic GSM were treated with the fractional CO_2 laser (MonaLisa Touch, DEKA) system across a series of treatments delivered at intervals of six or more weeks.

Results: A total of 102 women suffering from moderate to severe GSM were recruited. Eighty-four percent experienced significant improvement in their symptoms after CO_2 laser treatment. Scores on measures of sexual function, dyspareunia, and bothersomeness of sexual issues were improved from pre-treatment to long-term (12–24 month) follow-up. Furthermore, there were improvements on measures of bladder function (P = 0.001), prolapse (P = 0.001), vaginal sensation (P = 0.001), vaginal lubrication (P < 0.001) and urge incontinence (P = 0.003) from the pre-treatment assessment to the second assessment (i.e. after the third treatment).

Conclusions: In this study, fractional microablative CO_2 laser treatment was associated with an improvement in symptoms of GSM and sexual function.

CO2 LASER vs LOCAL OESTROGENS

Menopause: The Journal of The North American Menopause Society
Vol. 24, No. 7, pp. 824–830
DOI: 10.1097/GME.0000000000000955
© 2017 by The North American Menopause Society

Randomized, double-blind, placebo-controlled clinical trial for evaluating the efficacy of fractional CO_2 laser compared with topical estriol in the treatment of vaginal atrophy in postmenopausal women

Vera L. Cruz, MD,[1] Marcelo L. Steiner, MD, PhD,[2] Luciano M. Pompei, MD, PhD,[2] Rodolfo Strufaldi, MD, PhD,[2] Fernando L. Afonso Fonseca, PhD,[3] Lucila H. Simardi Santiago, MD, PhD,[4] Tali Wajsfeld, MD,[1] and Cesar E. Fernandes, MD, PhD[1,2]

- **Observational studies**
- **Up to 36 months**
- **n= 313**

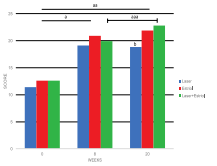


FIG. 2. VHI score of different treatment arms at multiple time-points. *Wilcoxon test $P < 0.05$, all groups; **Wilcoxon test $P < 0.001$, all groups; ***Wilcoxon test, LE week 8 vs week 20, $P = 0.01$; †Kruskal-Wallis test, L vs E and LE, $P < 0.05$; Friedman test for multiple time-points, $P < 0.001$, all groups.

CO2 LASER vs LOCAL OESTROGENS

Menopause: The Journal of The North American Menopause Society
Vol. 24, No. 7, pp. 824–830
DOI: 10.1097/GME.0000000000000955
© 2017 by The North American Menopause Society

Randomized, double-blind, placebo-controlled clinical trial for evaluating the efficacy of fractional CO_2 laser compared with topical estriol in the treatment of vaginal atrophy in postmenopausal women

Vera L. Cruz, MD,[1] Marcelo L. Steiner, MD, PhD,[2] Luciano M. Pompei, MD, PhD,[2] Rodolfo Strufaldi, MD, PhD,[2] Fernando L. Afonso Fonseca, PhD,[3] Lucila H. Simardi Santiago, MD, PhD,[4] Tali Wajsfeld, MD,[1] and Cesar E. Fernandes, MD, PhD[1,2]

TABLE 2. *Visual Analog Scale scores at 0, 8, and 20 weeks by treatment group*

	Laser (n = 15)	Estriol (n = 15)	Laser + estriol (n = 15)	P*
Dyspareunia				
Baseline	4.9 ± 3.7	3.2 ± 3.4	6.5 ± 3.9	0.09
Week 8	2.9 ± 2.9	0.6 ± 1.7	2.5 ± 3.8	0.16
Week 20	0.7 ± 1.5	0.2 ± 0.6	0.9 ± 1.8	0.95
P†	**0.01**	0.058	**0.009**	
Dryness				
Baseline	8.0 ± 2.6	5.6 ± 2.9	7.9 ± 3.0	0.07
Week 8	3.6 ± 2.6	2.4 ± 2.0	3.3 ± 2.9	0.57
Week 20	1.4 ± 2.0	0.5 ± 1.4	0.3 ± 0.7	0.35
P†	**<0.001**	**<0.001**	**<0.001**	
Burning				
Baseline	3.9 ± 4.5	0.9 ± 1.6	4.9 ± 3.8	**0.017**‡
Week 8	1.0 ± 2.0	0.1 ± 0.5	1.2 ± 2.7	0.33
Week 20	0.5 ± 1.5	0.1 ± 0.3	0.4 ± 1.1	0.95
P†	**0.02**	0.51	**0.002**	

Intention-to-treat analysis. Items listed as mean ± SD. *P* values of 0.05 were considered statistically significant.
*ANOVA.
†Friedman test.
‡Least significant difference analysis showed group E vs LE and E vs L: $P < 0.05$.
All others: Visual Analog Scale (0-10, where 0 = no symptom and 10 = severe symptom).

CO2 LASER vs LOCAL OESTROGENS

Randomized, double-blind, placebo-controlled clinical trial for evaluating the efficacy of fractional CO_2 laser compared with topical estriol in the treatment of vaginal atrophy in postmenopausal women

TABLE 3. *FSFI scores (individual domains and totall at 0, 8, and 20 weeks by treatment group*

	Laser (n = 13)	Estriol (n = 14)	Laser + estriol (n = 15)	*P*
Desire				
Baseline	2.4 [1.5; 3.6]	2.4 [2.1; 3.6]	1.8 [1.2; 3.0]	0.19
Week 8	2.4 [1.8; 3.6]	2.4 [2.2; 3.6]	3.0 [1.2; 3.6]	0.99
Week 20	2.4 [1.8; 3.6]	3.0 [2.4; 3.6]	3.6 [1.8; 3.6]	0.76
P (baseline vs week 20)[a]	0.39	0.63	**0.005**	
Arousal				
Baseline	2.4 [1.4; 4.0]	3.6 [2.1; 4.8]	2.7 [1.5; 4.5]	0.66
Week 8	2.4 [1.4; 3.4]	3.1 [2.0; 4.9]	3.6 [1.8; 4.2]	0.35
Week 20	3.0 [1.5; 3.6]	4.0 [2.2; 4.6]	3.9 [1.8; 4.5]	0.68
P (baseline vs week 20)[a]	1.00	1.00	0.17	
Lubrication				
Baseline	4.2 [2.7; 5.0]	4.2 [2.8; 5.6]	2.7 [1.2; 4.2]	0.15
Week 8	2.7 [1.0; 5.1]	4.5 [2.0; 5.1]	4.2 [2.7; 5.4]	0.49
Week 20	3.0 [0.8; 4.5]	3.9 [2.9; 5.2]	3.6 [2.7; 4.8]	0.29
P (baseline vs week 20)[a]	0.24	0.58	**0.02**	
Orgasm				
Baseline	4.0 [2.0; 4.8]	4.2 [2.9; 4.7]	3.6 [1.2; 4.8]	0.68
Week 8	2.8 [0.6; 4.4]	4.0 [0.0; 6.0]	4.0 [1.6; 5.6]	0.60
Week 20	2.4 [0.0; 4.6]	4.2 [2.3; 6.0]	4.4 [2.8; 5.6]	0.14
P (baseline vs week 20)[a]	0.26	0.95	0.11	
Satisfaction				
Baseline	3.2 [1.6; 4.8]	4.8 [2.1; 5.7]	3.6 [1.2; 4.8]	0.46
Week 8	4.0 [1.4; 4.8]	4.8 [2.3; 5.7]	4.8 [2.8; 5.2]	0.40
Week 20	3.6 [1.4; 4.0]	4.6 [3.0; 5.7]	4.8 [2.8; 4.8]	0.13
P (baseline vs week 20)[a]	0.72	0.60	0.09	
Pain				
Baseline	4.4 [1.6; 5.6]	4.8 [2.2; 5.7]	2.4 [1.2; 3.6]	**0.04**[b]
Week 8	2.0 [0.0; 4.4]	5.2 [0.0; 6.0]	3.6 [1.2; 4.8]	0.39
Week 20	2.0 [0.0; 3.6]	6.0 [3.9; 6.0]	2.8 [1.6; 5.6]	**0.006**[c]
P (baseline vs week 20)[a]	**0.04**	0.16	**0.02**	
Total				
Baseline	18.6 [16.4; 24.6]	23.6 [17.5; 29.8]	18.7 [7.2; 22.6]	0.21
Week 8	18.0 [11.4; 20.7]	22.9 [8.4; 29.7]	22.6 [11.3; 26.3]	0.39
Week 20	14.4 [7.8; 22.4]	25.4 [16.8; 29.3]	23.6 [14.9; 28.6]	0.10
P (baseline vs week 20)[a]	0.26	0.56	**0.02**	

CO2 LASER vs LOCAL OESTROGENS

Menopause: The Journal of The North American Menopause Society
Vol. 25, No. 3, pp. 27–28
DOI: 10.1097/GME.0000000000000955
© 2017 by The North American Menopause Society

Randomized, double-blind, placebo-controlled clinical trial for evaluating the efficacy of fractional CO_2 laser compared with topical estriol in the treatment of vaginal atrophy in postmenopausal women

Vera L. Cruz, MD,[1] Marcelo L. Steiner, MD, PhD,[2] Luciano M. Pompei, MD, PhD,[2] Rodolfo Strufaldi, MD, PhD,[2] Fernando L. Afonso Fonseca, PhD,[3] Lucilla H. Simardi Santiago, MD, PhD,[4] Tali Wajsfeld, MD,[1] and Cesar E. Fernandes, MD, PhD[1–2]

TABLE 4. *Parabasal cells (percentage per HPF) and Meisels (maturation value) at 0, 8, and 20 weeks by treatment group*

	Laser	Estriol	Laser + estriol	*P*[a]
Baseline				
n	12	11	10	
P cells	35.4 ± 31.5	45.3 ± 38.1	26.2 ± 36.3	0.47
Meisels	42.4 ± 24.0	36.9 ± 29.7	48.4 ± 25.3	0.61
Week 8				
n	12	14	13	
P cells	14.3 ± 24.4	2.4 ± 2.6	5.2 ± 8.2	0.11
Meisels	64.5 ± 23.1	65.6 ± 6.5	65.0 ± 10.5	0.98
Baseline vs week 8[b]				
P cells	**0.03**	**<0.01**	0.09	
Meisels	**0.01**	**0.01**	0.07	
Week 20				
n	11	9	11	
P cells	16.7 ± 29.2	6.1 ± 11.7	3.9 ± 3.7	0.24
Meisels	58.5 ± 23.7	58.2 ± 8.5	60.4 ± 8.6	0.93
Baseline vs week 20[b]				
P cells	**0.02**	0.11	**0.07**	
Meisels	**0.01**	0.46	**0.07**	